Author:
Molyneaux, Charlotte R R

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Cleft, the transverse dimension

CSAG vs CCUK

Cleft, the transverse dimension: CSAG vs CCUK.

Charlotte R R Molyneaux

BDS Hons (KCL), MJDF (RCS Eng)

School of Oral and Dental Sciences

University of Bristol

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ABSTRACT

Introduction: Since the recommendations put forward by the Clinical Standards Advisory Group (CSAG) 1998 have been adopted by the cleft community, training, caseload and cleft team composition have undergone significant change. The improvements in cleft outcomes have been well documented by the subsequent Cleft Care UK (CCUK) study. Whilst the changes in dentoalveolar relationships have been assessed, the transverse dimensional changes are less well reported. The aim of this study was to determine if the transverse dimensions of maxillary unilateral cleft lip and palate affected children has improved since the implementation of the CSAG recommendations.

Methods: Maxillary models from each of the CSAG (114) and CCUK (175) cohorts were digitally scanned and anonymised. Linear and angular measurements were taken including; the intermolar width and intercanine width, the distance to the midline for each of the primary canines (C) and second primary molars (E), anterior depth and posterior depth, arch length and arch form angles between the two populations, CSAG and CCUK. The data was then analysed using Stata statistical software and described with respect to the cohort and the side (cleft affected or not).

Results: Statistically and clinically significant differences were observed between the CSAG and CCUK cohorts for the affected side C, affected side E and posterior width measurements with the means of the CCUK cohort (11.09mm, 20.53mm, 41.19mm respectively) being greater than the CSAG cohort (10.05mm, 19.50mm, 39.96mm respectively). Neither statistically or clinically significant differences were observed for the non-affected side C, non-affected side E, posterior depth, arch length or arch form angles. Differences were seen

in the linear and angular measurements when the cleft affected and non-affected sides were compared.

Conclusion: The study has found improvements for the measured outcomes for children born with unilateral cleft lip and palate in more recent years. Although clear differences remain between the cleft affected and not affected sides of the maxilla, within the CCUK cohort the arch widths are closer to the norms for unaffected children.

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AUTHOR'S DECLARATION

I declare that the work in this dissertation was carried out in accordance with the requirements on the University's Regulations and Code of Practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidates own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

SIGNED

DATE

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GLOSSARY

CCUK	Cleft Care UK
CLP	Cleft lip and palate
CL	Cleft Lip
CL/P	Cleft lip and/ or palate
CP	Cleft Palate
CSAG	Clinical Standards Advisory Group
MDT	Multidisciplinary Team
UCLP	Unilateral cleft lip and palate
BCLP	Bilateral cleft lip and palate

1.INTRODUCTION

An investigation into the standard of care and outcomes of children born in the UK with a cleft lip and/ or palate by the Clinical Standards Advisory Group (CSAG) reported to the UK government in 1998 (CSAG 1998). Following this, recommendations put forward by CSAG have been adopted by the cleft community, training, caseload and cleft team composition have undergone significant change. A subsequent study set up in 2011 entitled Cleft Care UK (CCUK) documented improvements in cleft care for a multitude of outcomes (Ness *et al.* 2017). As part of these, occlusal outcomes were assessed for five-year olds using the 5-Year Olds' Index (Atack *et al.* 1997). Although the antero-posterior outcomes have been previously studied (Al-Ghatam *et al*. 1995), the maxillary transverse dimensional changes in isolation are less well reported.

2.REVIEW OF THE LITERATURE

Cleft care in the United Kingdom has undergone significant changes in the last 10-15 years and several metrics have indicated that these changes have been of significant benefit.
The goal of surgically treating dentofacial anomalies, such as cleft lip and/ or palate (CL/P), is to produce a harmonious facial appearance, with minimal residual asymmetry (Bell *et al.* 2014), and a successful reconstruction of the palate, lip and alveolus that promotes functional development. Ideally a lay individual would not notice that the child had been born with a cleft at the age of five years.
Therefore, this review will include the aetiology and epidemiology of CL/P, followed by interrogation of the literature about children born with CL/P, and the recommended

provision of cleft care in the UK following the 1998 Clinical Standards Advisory Group (CSAG) review. The findings of the Cleft Care UK study will be described along with a comparison of the CSAG data. The surgical methods and measurement techniques for the treatment outcomes will also be described.

2.1 Cleft Lip and / or Palate

Children born with clefts of the lip and / or palate are estimated to be one in 700 live births within the UK (Coupland and Coupland 1988, Gregg et al. 2008, Bellis and Wohlgemuth 1999), making this one of the commonest congenital craniofacial abnormalities worldwide (World Health Organization in the World Atlas of Birth Defects (WHO 2003). Facial clefting may be isolated or a component of syndromes such as Pierre Robin sequence, 22q11 deletion, Stickler and Van de Woude.

Diagnosis of a cleft lip is now commonly made during pre-natal scans and in one study of 103 foetuses with oral cleft, the mean gestation time at detection was 20.4 weeks (Maarse *et al*. 2015). The full extent of the cleft, and indeed the condition itself, may not be apparent until birth. Increased understanding of the genetic contributions to clefting may provide further specific testing and enable early diagnosis of syndromic and non-syndromic cleft lip and / or palate.

A child born with a cleft will require treatment from birth to the early years of adulthood and potentially beyond. There may be complications with feeding, hearing, speech, facial and dental development. Commonly these issues may be accompanied by psychosocial problems. Successful outcomes require multidisciplinary, highly specialised care (Colbert *et al.* 2015).

2.1.1 Epidemiology

The prevalence of CL/P shows geographical variation, some of which can be attributed to variation in effective reporting. Isolated cleft palate is the most common form of clefting and is more common in females (Coupland and Coupland 1988), whereas cleft lip with or without cleft palate is more common in males, and unilateral clefts are at least twice as common as bilateral clefts. Isolated cleft lip accounts for around 25% of all clefts. Unilateral cleft lip or cleft lip and palate occurs more frequently on the left side in a ratio of 2:1 (Gregg *et al.* 2008).

Combined data from European registries for 1995 to 1999, showed 3.5% of babies with cleft lip, with or without cleft palate, were stillborn and 9.4% were from terminated pregnancies (Dolk 2005). Recent work from the Netherlands suggests that following the introduction of antenatal screening for clefts, the number of cleft births has reduced due to mothers opting to terminate the pregnancy. The authors suggest that this trend for a decline in prevalence is most likely due to termination of pregnancy for multiple congenital anomalies, including CL/P. This is because the termination of pregnancy rate for isolated CL/P remains low (Mink van der Molen *et al.* 2011).

2.1.2 Facial Development

Facial development results from neural crest cell infiltration and mesenchymal proliferation that forms swellings in the facial region of the embryo. These facial primordia grow, merge and fuse to become the facial structures. The mesenchymal tissues are bounded by undifferentiated epithelium and in order for them to fuse the epithelial barrier must be lost. In CL/P this fusion does not occur, leading to a developmental abnormality which may affect

the lip, alveolus, hard or soft palate, or a combination of these sites. This abnormality may be uni- or bilateral.

Normal facial development is first identified at around 24 days *in utero* when the frontal maxillary and mandibular processes become apparent. First to unite are the mandibular processes, at 31 days *in utero*, giving rise to the lower lip, cheeks and other mandibular structures. The upper lip is formed from the median nasal process centrally and the maxillary processes laterally, and fusion should occur at 6 weeks *in utero*. The medial nasal process will also develop to form the philtrum, primary palate, upper incisor teeth and alveolar bone. The secondary palate is formed from the down-growth of the palatal shelves. During weeks 7-8 *in utero,* the palatal shelves elevate to a horizontal position above the tongue. This is a rapid movement, which may take place over minutes or hours. Both intrinsic and extrinsic mechanisms have been described, but the true mechanism remains unknown. However, each step of palatogenesis, from initiation until completion, is subject to tight molecular control that is governed by epithelial–mesenchymal interactions (Gritli-Linde 2007). Following elevation, further growth of the palatal shelves brings their medial edges into contact. Apoptosis of epithelium, transformation of epithelium to mesenchyme, or migration of epithelium, are all possible mechanisms leading to fusion of the shelves. This fusion is also seen between the secondary and primary palates. This process results in a physical divide between the oral and nasal cavities and is complete by the 10^{th} embryonic week (Berkovitz *et al.* 2009).

In CL/P the failure of fusion between some or all of these components results in clefting. The cleft can be complete, incomplete, unilateral (UCLP) or bilateral (BCLP) depending on the extent of failure of fusion.

2.1.3 Aetiology

Cleft aetiology is thought to be multifactorial, implicating both genetic and environmental factors. The interaction of these two aetiologies at specific time points during embryogenesis is likely to affect the development of the face.

Europe wide, approaching 30% of those born with a CP also presented with a recognised condition (Calzolari *et al.* 2004). Syndromic clefting often has a greater tendency for bilateral clefts. More than 400 syndromes have been identified as being associated with CL/P.

Various genes have been associated with syndromic and non-syndromic CLP. The advent of genomics has led to significant advances in identifying the causative genes for syndromic clefts (Online Mendelian Inheritance in Man https://ncbi.nih.gov/omin) and has also increased the understanding of the genetic aetiology of non-syndromic CLP (Dixon *et al.* 2011). Mutations in *IRF6* have been identified as causal in Van der Woude syndrome (Cobourne 2004). Also shown to be associated are *SOX9* in Pierre Robin (Benko *et al.* 2009),*TCOF1* in Treacher Collins (Treacher Collins Syndrome Collaborative Group 1996) and *TBX1* in Di George syndrome (Packham and Brook 2003).

A recent study by Carson *et al.* (2017), across 13 countries, describes the mounting evidence to suggest that two different phenotypes may be responsible for two common subtypes, namely cleft lip alone (CL) and CL with cleft palate (CLP) in non-syndromic cleft lip. This contradicts the previous assumption that a single phenotype was responsible. Consequent to this they identified a region on 16q21 that is strongly associated with cleft lip over cleft lip and palate phenotypes.

Environmental factors that have been linked to CLP include maternal exposure to tobacco smoke, alcohol, poor nutrition, viral infection, medicinal drugs and teratogens in early pregnancy (Mossey *et al.* 2009). Maternal smoking is known to increase the risk of CL/P and isolated cleft palate (CP) (Little *et al.* 2002), whereas maternal consumption of alcohol does not have equally strong evidence of association with clefting. Dietary supplements are commonly taken in pregnancy. The use of multivitamins in relation to cleft has been investigated, particularly in relation to zinc and folate. Mothers of children with CLP in the Netherlands were found to have lower concentrations of circulating zinc than mothers of children without clefts (Krapels 2004). The intake of folate in early pregnancy has been linked to decreased risk of orofacial clefts (Johnson and Little 2008). Folate deficiencies are known to be important in foetal development and have been found to associated with clefts in animal studies (Munger & Wyszynski 2002).

2.1.4 Types and classification of clefts

Clefts may be described as either incomplete or complete, unilateral or bilateral and affecting the lip, alveolus, hard or soft palate. A range of presentations within these can be seen in the cleft affected population, as shown in Figure 1.

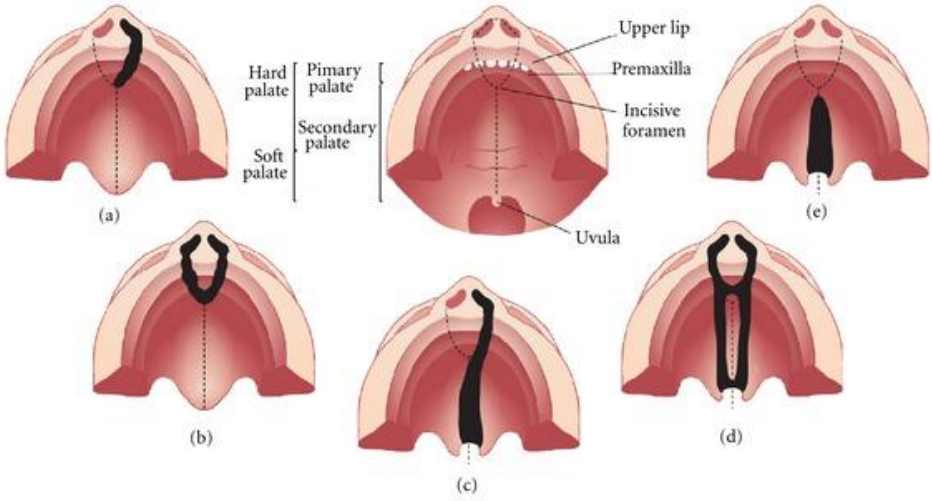

Figure 1: Diagrammatic representation of types of cleft lip and palate (a. unilateral cleft lip with alveolar involvement, b. bilateral cleft lip with alveolar involvement, c. unilateral cleft lip associated with cleft palate, d. bilateral cleft lip and palate, e. cleft palate only) (Source: Brito *et al.* 2012 p3.)

Many formal classifications have been described. The 'LAHSHAL' (lip, alveolus, hard palate, soft palate, hard palate, alveolus, lip) text-based terminology is often used within the UK and describes the structure affected, whether it is complete or incomplete, including laterality. Figure 2 is a diagrammatic representation of the LAHSHAL classification.

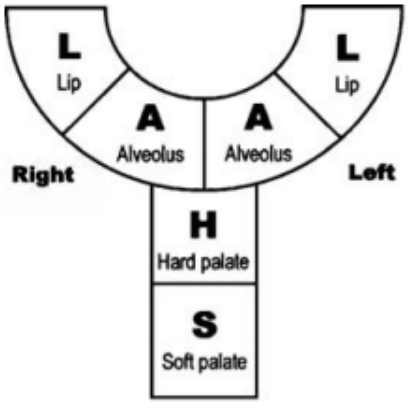

Figure 2: Diagrammatic representation of the 'LAHSHAL' terminology. (Source: Shah *et al.* 2011 p97)

Example of how the LAHSHAL classification works are:

- 'LAHS..' is complete right side unilateral cleft affecting the lip, alveolus, hard and soft palate.
- '….l' is left sided incomplete cleft lip.

2.1.5 Comorbidities and Quality of Life with CL/P

Foetal ultrasound detection can mean the impact of CL/P is present before birth for the parents and through to adulthood for the individual affected. Despite improvements in surgical corrective techniques, many children commonly experience a range of associated difficulties. These include chronic ear infections, problems with growth, abnormal development of the dentition (with missing and malpositioned teeth), speech and language development. Glue ear, Class III malocclusion, dental caries and hypernasality are all associated comorbidities.

The impact on quality of life for non-syndromic CLP depends on the extent of the phenotype expression. Function is the first hurdle, as initially feeding may be problematic because the

infant is unable to form an adequate lip seal for sucking. Feeding adjuncts such as specialised bottles and teats are available.

Adverse cognitive and intellectual effects have also been observed in children born with CL, CP and CLP. In a meta-analysis, people with any type of cleft display moderate to significant deficits in immediate memory, language and attention/executive abilities. However, a moderate deficit in the language domain was the only area which was based on non-heterogeneous study findings and not subject to publication bias (Roberts *et al.* 2012). Psychological and psychosocial wellbeing of individuals born with CLP have also been examined.

A prospective multi-centre study in France showed that 60% of 12-year olds reported suffering from taunting and peer victimisation at school, and in 84% of cases this was linked to the cleft itself (Larot-Marchand *et al*. 2015). A systematic review found most children and adults with CLP do not appear to experience major psychosocial problems, but difficulties have been reported in relation to behavioural problems, satisfaction with facial appearance, depression and anxiety (Hunt *et al.* 2005). A more recent qualitative study (Hamlet and Harcourt 2015) reported that an older adult population seemed at ease living with CL/P and considered it an important aspect of their identity. However, they did report that health care could be more considerate, particularly dentistry and information provision.

2.1.6 Clinical Pathway of Cleft Care

Within the UK there is a routine pathway of cleft care from prenatal diagnosis to early adulthood. This is well established, and all care is provided by a specialist cleft team. The aims of treatment, intervention and support are to restore normal function and allow for

normal development. The most common treatment and interventions are described in Table 1, along with the team members involved at each stage.

Stage	Age	Intervention			Team Members
Diagnosis and Birth	Prenatal to 3 months	Contact from cleft specialist nurse. Introduction to the service. Feeding advice. Counselling.		Psychological support including clinical geneticist	Sonographer Cleft specialist nurse. Clinical psychologist
1st Year	3-6 months	Primary lip repair.			Primary cleft surgeon
	6-9 months	Primary palate repair.	Preventative dental care		Primary cleft surgeon
Early Years	1-4 years	Formal speech and language assessments			Speech and language therapist.
		Audiology Assessment			ENT surgeon
School Years	5-12 years	Formal cleft MDT assessment at 5 and 10 years			MDT
	8-12 years	Alveolar bone graft			Secondary cleft surgeon
Teenage Years	13-18	Orthodontic treatment			Orthodontist
Early Adulthood	>18	Orthognathic Surgery (if required)			Cleft Maxillofacial Surgeon and Orthodontist
		Rhinoplasty (if required)			Cleft Maxillofacial Surgeon
		Definitive restorative dentistry			Restorative dentist

Table 1: Routine care pathway for a child born with CLP. (Abridged from CLAPA.)

The care provided will be individualised to each patient. Support from specialist nursing and speech and language therapy can often continue throughout childhood. Some people will require longer and more intensive intervention from specific care providers. The intensity of the care received by these children is such that they could undergo three significant surgical procedures by the age of 12 years. There is also the possibility of later revision surgery and pharyngoplasty if required.

2.2 Clinical Standards Advisory Group (CSAG) Cleft Lip and Palate Study

2.2.1 Background

Following the 1985 Fifth International Congress on Cleft Lip and Palate and Related Craniofacial Abnormalities, researchers agreed to undertake an international comparative study of UCLP. This multi-centre study allowed direct comparisons between primary surgery outcomes, examining craniofacial morphology, dental arch relationships and nasolabial appearance (Shaw *et al.* 1992a). The two UK centres included in the study reported worse outcomes than the other four international centres. Procedure, standardisation, centralisation of care and high-volume operators were associated with good outcomes, whereas non-standardisation and low-volume operators were associated with poor outcomes (Shaw *et al.* 1992b).

These findings and those of a previous study, which also demonstrated shortcomings in UK cleft care (Mars *et al.* 1987), provided clear drivers for change in the UK cleft service. Similarly, health care professionals were concerned about the quality of care for children born with CLP in the UK, as were parents and consumer groups. (Sandy *et al.* 2001).

Prior to 1998, cleft care in the UK was fragmented, with 57 centres and 78 surgeons providing care for approximately 1000 children / year. Only seven surgeons repaired five or more unilateral CLP/year at this time (Colbert *et al.* 2015).

2.2.2 CSAG Investigation

The Clinical Standards Advisory Group (CSAG), was commissioned by the UK government in 1996 to examine care provided for people born with CLP, along with the training of those delivering that care in the UK. A retrospective comparative study of 239 five-year olds and 218 12-year olds born with UCLP was conducted. Outcome data included study models, lateral cephalometric and anterior occlusal radiographs, clinical photographs, oral health assessment, speech and satisfaction with care. With regard to delivery of training, recently appointed cleft team members were surveyed to evaluate their experience of providing cleft care. Senior cleft surgeons and orthodontists were also invited to consider the organisation of future training and progression along a cleft training pathway.

The 5-year-olds were chosen as being the first opportunity at which the outcome of primary surgery could be assessed, without the influence of orthodontics or bone grafting. Thereby providing an early indication of variations in clinical practice. The 12-year-old cohort was chosen so that the success of secondary alveolar bone grafting and facial growth could be evaluated. A total of 601 children were invited to participate from the 50 cleft centres that were willing to be involved. The recruitment rate to the study was 76% of those invited. (Sandy *et al.* 2001)

2.2.2.1 CSAG Outcome Measures

A 'Cleft Team Questionnaire' was developed to assess the surgical and clinical facilities as well as access to different specialties at each cleft care centre. Forty-eight of the 57 teams completed the survey. The main outcome measures used are listed in Table 2. With respect

to training, a sample of recently appointed cleft team members were surveyed to evaluate their experience of cleft care.

Outcome measures recorded	
Dentofacial outcomes	Speech outcomes
• skeletal pattern • dental arch relationship • success of alveolar bone grafting • facial appearance • oral health status • patient/parent satisfaction	• intelligibility • nasality • ‘‘speech cleft type characteristics’’ • speech therapy intervention

Table 2: Clinical and non-clinical outcome measures used in the 1998 CSAG study.

2.2.2.2 Findings of the CSAG Investigation

The results of the CSAG study are summarised below.

Dentofacial outcomes including skeletal relationship, success of alveolar bone grafting, facial appearance and oral health assessment, as well as patient/parent satisfaction were reported by Williams *et al.* (2001).

Skeletal relationship/pattern was assessed using lateral cephalogram radiographs. It was found that:

- 70% of those receiving treatment at participating cleft centres had a class III skeletal relationship (ANB < 2^{o})

- 50% had marked class III skeletal relationship (ANB < 0^o)
- 17% were skeletal class I (ANB 2^o to 4^o)
- 13% were skeletal class II (ANB > 4^o)

Population norms would usually only see 3% as having a marked skeletal III relationship. (Cohen and Horowitz 1970). Two European studies reported occlusal relationships in non-cleft populations to be:

- 71% & 69% class I
- 23% & 28% class II
- 2% & 5% class III (Ingervall *et al.* 1978 and Salonen *et al.* 1992)

Dental arch relationships were assessed using dental study models and the 5-Year Olds' Index (Atack *et al.* 1997) and Goslon Yardstick (Mars *et al.* 1987). The results showed that 37% of five-year-old models and 39% of 12-year-old models were in the ''poor'' or ''very poor'' categories for occlusion. The aim of these somewhat subjective indices (Atack *et al.* 1997 & Mars *et al.* 1987) was to provide sound data to surgeons, enabling judgment of their surgical results and whether modification of the current surgical technique was justified.

Successful alveolar bone grafting was assessed using an anterior occlusal radiograph. Whilst it would be expected that all 12-year olds should have undergone alveolar bone grafting by this age, 15% of the 12-year-old cohort had still not received a bone graft and only 58% of bone grafts were rated as successful.

Facial appearance was assessed using clinical photographs cropped to focus on the nasio-labial appearance. The examiners found that only 31% of five-year olds and 20% of 12-year

olds had a good or very good lip appearance, and only 31% of five-year olds and 25% of 12-year olds had a good or very good nasal appearance. For five-year olds and 12-year olds respectively, their profile was judged to be fair in 48% and 49% of cases.

Oral health assessments were undertaken by orthodontists. Most patients (>95%) were registered with a dentist. Even so, 40% of five-year olds and 20% of 12-year olds were believed to need treatment for dental caries. Also, 39% of 5-year olds and 10% of 12-year olds had a symptomatic, persistent oral fistula.

Overall satisfaction with care was measured using a self-report questionnaire completed by parents:

- 67% of parents felt they received excellent ‘‘care and attention’’ from the cleft team
- 6% were dissatisfied with “care and attention”
- 56% felt that the ‘‘treatment and outcome’’ of care had been excellent
- 35% thought that care was ‘‘good’’
- 9% were dissatisfied with the overall outcome.

In terms of speech intelligibility (Sell *et al.* 2001), most 12-year olds (81%) were judged to have intelligible or slightly different speech, but 4% of 12-year olds and 19% of 5-year-olds were judged to have speech that was impossible to understand, or ‘‘only just intelligible to strangers.’’

At the time of the study a proportion of children had already undergone secondary velopharyngeal surgery. This cohort, along with those presenting with consistent hypernasal resonance, provides the estimate that 29% of 5-year olds and 32% of 12-year-olds had an

inadequate primary repair in terms of velopharyngeal function. A further need for speech therapy was recorded for 46% of 5-year olds and 15% of 12-year olds who were not currently receiving it.

These findings gave '*cause for concern'* (Sell *et al.* 2001) for cleft care in the UK, both in the surgery received and the ongoing support for speech and the maintenance of dental health. It was felt that cleft provision was not meeting the needs of the population at this time.

2.2.2.3 Conclusions of CSAG

In terms of clinical outcomes and service infrastructure, the CSAG investigation (Bearn *et al.* 2001) concluded that:

- High volume of surgery was associated with better outcomes for approximately one third of key variables, and there were no instances in which low volume was associated with better outcome.
- Unless a sufficient volume of patients are being treated in a centre, and appropriate records are kept, the quality of cleft care could never be verified over a reasonable time period.
- Some services were unable to pay for, or provide a comprehensive range of specialists and resources.

With respect to training:

- Sixty percent of orthodontists reported that their training could have been improved with greater experience.

- Not all had undertaken “normal” procedures during training that would be carried out when treating cleft patients on a day-to-day basis.
- Nearly all of the plastic and maxillofacial surgeons felt their training could have been improved, and the majority felt that surgical experience needed to be more closely supervised.
- Sixty percent of new and experienced speech and language therapists had only received undergraduate training. None of those recently appointed had attended courses on cleft care.

2.2.2.4 CSAG Recommendations

The CSAG 1998 made eight specific recommendations via the ‘Report of a CSAG Committee’ to overhaul practice (Bearn *et al.* 2001 page 42), namely:

1. Expertise and resources in the UK should be concentrated in 8 to 15 centres instead of the 57 in place at that time.
2. The range of expertise required in the team and the quality of standards required should be clearly indicated by purchasers of care.
3. Units providing cleft care should ensure that the full range of skills are available.
4. Clinicians should agree on a common nationwide database for all cleft patients.
5. Information on all cleft patients should be made available for comparative studies.
6. Training programmes for all specialist cleft clinicians should be provided only in cleft centres at which high-volume and high-quality clinical experience is available.
7. The surgical specialties involved must develop a common training pathway for the small number of trainees required to specialise in cleft care.

8. The Office of National Statistics should improve the recording of cleft births.

2.2.2.5 Government Response

The UK Government accepted the CSAG 1998 report recommendations in full and gave the NHS Executive responsibility for immediately setting up the Cleft Implementation Group. It was recommended that cleft care should be rationalised into 'hub and spoke' regional centres, where teams could treat larger numbers of patients following formal service specifications. The 'hub' being the central operating site, supported by 'spoke' outpatient services. Emphasis was placed on considerations for quality, effectiveness and the potential for audit to monitor progress and improvement.

Centralisation took time, with 10 centres designated and recruiting teams by 2005 (Hodgkinson *et al.* 2005), seven years after publication of the CSAG report. Ten years on from this, Colbert *et al.* (2015) described the contemporary management of cleft lip and palate care in the UK. At this time, cleft services were managed through clinical networks led by a clinical director. Each regional centre had a multidisciplinary team treating a minimum of 80 babies each year, remaining within the service until at least the age of 20. New referrals of adults previously treated by the former cleft service would not be uncommon. These patients often present with additional challenges surgically, clinically and emotionally. Surgeons must have completed designated training and treatment following evidence-based guidelines and national policies. (NHS Commissioning Board 2013)

2.3 Cleft Care UK (CCUK)

The CCUK study investigated the clinical impact (*i.e*. patient outcomes) of reconfigured cleft services in the UK, 15 years after centralisation of care was recommended in the CSAG

report. It was a UK wide, multicentre cross-sectional study of 5-year-olds (n = 268) with non-syndromic UCLP, who were born between 1 April 2005 and 31 March 2007. In the CCUK study, recruitment and clinical measures were conducted in such a way as to replicate the earlier CSAG study as closely as possible (Persson *et al.* 2015), making the studies comparable. Outcome measures included:

- Surgical treatment
    - type of primary lip and palate repair and any complications
    - presence of oral fistulae
    - subjective rating of surgical outcome
- Dental arch relationship
    - alginate impressions with wax squash bite and/or intraoral photographs
    - assessed with the 5-Year Olds' Index
- Facial aesthetics
    - profile and frontal photographs standardised and cropped to nose and lip area
    - rated independently by a panel of assessors
    - parents' perception of appearance by a Satisfaction with Appearance Scale
- Oral Health
    - Decayed missing filled teeth (dmft) score
    - Reported from parental accounts and hospital notes
- Audiology
    - Reported from parental accounts and hospital notes
    - Full audiogram
- Somatic Growth

    - Child's height, weight and head circumference
- Speech
    - Speech and language therapy history questionnaire
    - History of velopharyngeal insufficiency and surgery
    - Estimate of residual need for therapy
    - Use of Cleft Audit Protocol for Speech-Augmented tool (nasality, nasal airflow, cleft speech characteristics, intelligibility)
- Psychosocial factors
    - Modified 18 item standardised questionnaire to assess parental/guardian perceptions of the impact of the cleft on their child
    - The 35 item Strength and Difficulties Questionnaire (Goodman *et al.* 1998)
- Health and lifestyle
    - Three questionnaires collecting basic demographic data (ethnicity, parental age at birth, parental education and parental occupation)
- Satisfaction with service
    - Questionnaire to assess parental satisfaction with the cleft service

Data were obtained for most clinical outcomes in 90% of the participants and the results of their findings are summarised in Table 3.

Al-Ghatam *et al.* (2015) reported that the increased caseload for each surgeon was associated with observed clinical improvements for individuals (facial and dento alveolar outcomes). Surgeons were required to undergo a cleft specific training program and 17/19 primary surgeons operated on 40-50 cases per year. They also suggested that the

established audit culture encourages sharing of results, links practice with outcomes and promotes reflective practice among teams. The improvement in 'excellent' or 'good' dentoalveolar relationships is likely to be due primarily to improved surgical technique, as the 5-year-olds assessed had not undergone alveolar bone grafting or reached full facial development.

In response to poor outcomes for dental caries, Smallridge *et al*. (2015) highlighted the lack of a paediatric dentist attached to 6 of the 11 regional cleft units, citing a failure to persuade commissioners that a paediatric dentist was required for the MDT. In only three regions was a paediatric dentist in regular attendance at the MDT.

Regarding speech outcomes, Sell *et al.* (2015) also compared the CCUK and CSAG outcome data. They noted differences in the methods used between the two studies due to evolution of the specialty and how outcomes are measured. However, even after accounting for these differences there was still strong evidence that speech outcomes were better for a greater proportion of CCUK children compared to CSAG children. These improvements may be attributed to the development of multidisciplinary teams within the cleft service, but variation is seen across cleft centres, potentially due to different practices or available resources. However, parameters which did not show improvement were nasal emission, nasal turbulence, hyponasality and lateral/lateralisation. Importantly, there remains a group of school entry children whose speech is unintelligible. This requires further study in order to understand and identify where resources should be allocated to further improve speech at age seven (Ness *et al*. 2017).

Waylen *et al.* (2015) reported on satisfaction of cleft services and psychosocial outcomes associated with appearance and speech using two questionnaires. Fewer parents in the CCUK study (8%) perceived their children as having poor self-confidence compared to CSAG

(18%). However, ten percent of parents felt their children had experienced teasing or bullying about their cleft, although unfortunately this had not been included in the original CSAG study. On the other hand, centralisation of care was not associated with an increase in families finding it difficult to attend appointments. Similarly, general levels of satisfaction with care remained high (98%), as was seen with CSAG (93%).

The Cleft Care UK study (Ness *et al.* 2015) found that whilst some outcomes (facial growth, speech, and parental report of self-confidence) had improved after CSAG, others (dental health and hearing) had not. It is also important to remember that a proportion of children still have poor outcomes despite centralisation. In conclusion, it was suggested that monitoring of the current centralised model of care is required to ensure the best outcomes for all children with CLP, to maintain an environment of sharing results and promote ongoing improvement.

Outcome measure		CCUK 2015 Result (%)	CSAG 1998 Result (%)	Conclusion
Dento-facial outcome (Al-Ghatam *et al.* 2015)	Excellent or good facial appearance Poor or very poor facial appearance Excellent or good dentoalveolar relationships Poor or very poor dentoalveolar relationships	36.2 21.6 53.0 19.2	31.9 27.6 29.6 36.3	Facial and dento alveolar outcomes were better in CCUK than CSAG.
Oral health and audiology (Smallridge *et al.* 2015)	Caries free Untreated caries At least one set of grommets Abnormal middle ear status	48 44.7 43 50.7	45 25.4	Outcomes for dental caries and hearing were no better than in CSAG, despite reduced use of grommets and greater used of hearing aids.
Perceptual speech outcomes (Sell *et al.* 2015)	Intelligibility, hypernasality, palatal/palatalization, backed to velar/uvular, glottal, weak and nasalized consonants. Nasal emission, nasal turbulence, hyponasality, lateral/lateralization.	Improved No improvement		Improvements in speech outcomes after CSAG.
Psychosocial outcomes and satisfaction with cleft service. (Waylen *et al.* 2015)	Perception of poor self confidence Satisfaction with appearance Satisfaction with treatment received Satisfaction with care	8 81 not reported 98	19 not reported 89 93	Improvements in some parental perceptions, but little difference in already high levels of satisfaction with cleft services.

Table 3: Summary of results and conclusions from CCUK 2015 study

2.4. Surgical Repair of Cleft Lip and Palate

In repairing the lip and palate of affected children the goal is to provide more normal function, structure and aesthetics, whilst minimising the adverse effects of surgery. The failure of fusion of the involved structures results in unopposed muscle contraction, causing deviation, widening and flattening of the nose and mouth. The primary repair of the lip is undertaken around 3 months, the palate at 9 months and the alveolus maybe at the time of palatoplasty or secondary bone grafting at around 8-10 years. The repair must create a functional replacement of the pan oral musculature.

2.4.1 Surgical Techniques

There have been multiple surgical techniques described to close lip clefts. All involve incisions along the margin of the extra and intra oral tissues of the cleft to create flaps of skin, muscle and mucosa, which are then brought together in various patterns and sutured closed to recreate typical lip and nose anatomy. For the palate, again incisions are made along the length of the cleft, with or without relieving incisions, allowing for the two sides to be brought together in a three-layer closure (nasal mucosa, muscle and oral mucosa). The repair is then closed with sutures, providing enough length of the palate to allow for normal feeding, speech development and continued growth throughout life.

For repair of the lip, techniques that have been described include the Millard and Delaire techniques, which both recognise the importance of repositioning the orbicularis oris muscle (van de Ven *et al.* 2008), recreating lip length and alignment of the vermillion border. The decision as to which technique to use depends on the extent of the cleft and surgical preference.

Commonly in the UK a vomer flap is also performed at the time of lip repair, which seals the cleft of the anterior hard palate. This is in line with the Oslo protocol for cleft repair.

Vomer flaps can be used with modifications to close the anterior hard palate in both unilateral and bilateral clefts. In an analysis by Agrawal and Panda (2006), vomerine tissue had been used in 1000 cleft cases over 17 years. Of the 678 patients with comprehensive records, fistula rate at the hard and soft palate junction was 2.95%. They stated, *"Although facial growth pattern was not recorded, obvious midface growth abnormalities were not observed in any of these patients."*

Palatal repair (palatoplasty) would ideally give perfect feeding and speech development, without affecting the maxillofacial growth and hearing. Principles of palatal repair have been set out by Agrawal (2009) and include:

- Closure of the defect
- Correction of the abnormal position of the muscles of the soft palate.
- Reconstruction of the muscle sling.
- Retropositioning of the soft palate, so that during speech the posterior part of the soft palate comes in contact with the posterior pharyngeal wall.
- Minimal or no raw area should be left on the nasal side or the oral surface.
- Tension-free suturing.
- Two-layer closure in the hard palate and a three-layer closure of the soft palate (nasal, muscle and oro-mucosal).

Cleft palate repair techniques have been described since 1861 with the von Langenbeck technique of palatal closure. Whilst still used for cleft palate only closure, the following techniques described to close a cleft palate are an evolution of this method.

Veau-Wardill-Kilner palatoplasty had been a very common technique, however full mucosal coverage is not achieved and exposed bone is left to heal via secondary intention. This can result in velopharyngeal incompetence, alveolar arch deformity and dental malalignment (Agrawal 2009). Friede *et al.* (1991) found that this style of push-back closure of the palate impaired maxillary development, both antero-posterior and transverse, compared with patients operated on using the von Langenbeck method. This technique has therefore fallen out of favour.

The Furlow Double Opposing Z-Plasty (Furlow 1986) aimed to improve speech results whilst allowing for normal maxillofacial development. The technique was described for use in unilateral, bilateral and cleft palate only. Whilst there is reported improvement in speech outcomes, limited objective evidence is available. This technique is no longer used in the UK.

A two-stage palatoplasty was developed in an attempt to limit the effect of hard palate closure on maxillary hypoplasia, with the hard palate repair occurring between 10 and 12 years of age, the soft palate having been repaired between four to six months. This resulted in a reduced width hard palate cleft, which was easier to repair and reduced maxillary hypoplasia (Schweckendiek & Doz 1978). However, speech outcomes were poor so this method had limited longevity and subsequently is no longer is use. The 2014 review by Farronato *et al.* endorses this.

One-stage cleft lip and palate repair is a technique primarily used in developing countries where multiple hospital admissions have limited feasibility. This technique is performed at

around three months of age and aims to completely close the anterior hard palate and alveolus along with the cleft lip. In a series of 61 patients, 58 had complete and stable closure of their anterior palate and alveolus after 1 year and there were only three incidences of fistula formation (Lehman *et al.* 1990). However, a retrospective comparison study from 2015 examined the outcomes of the one stage and two stage UCLP repair (Fudalej *et al.* 2015). This found that the two-stage group showed more favourable outcomes in the cephalometic variables that were measured. Furthermore, primary alveolar bone grafting has shown worse outcomes in both the Americleft (Daskalogiannakis *et al.* 2011) and Eurocleft (Shaw *et al.* 2005) studies.

The Bardach two-flap palatoplasty, first described in 1967, allows for two-layer closure in the hard palate and a three-layer closure of the soft palate via precise dissection of soft palate muscles and nasal periosteum. This creates lengthening of the soft palate and increased mobility, with normal speech production being reported in 75%-80% of patients (Bardach 1995). This technique is favoured in the USA.

Carsten (1999) describes the Alveolar Extension Palatoplasty technique, which priorities blood supply to the cleft side isolated tissue. Carsten claims that this is expected to reduce maxillary hypoplasia.

Nowadays in the UK, the most common technique is a modification of the Von Langebeck, reconstructing the palatal muscles via intravelar veloplasty. This can be completed with or without relieving incisions, depending on the width of the cleft and the elasticity of the palatal mucosa.

Gingivoperiosteoplasty is used to repair the cleft in the alveolus by creating a mucoperiosteal bridge across the cleft. Completed in conjunction with palatal repair, the aim of this is to allow for bone generation within the alveolus along with normal dental

development, avoiding the need for bone grafting later in life. Evidence for the success of this is limited. Wojtaszek-Slominska *et al.* (2010) compared 120 non-syndromic UCLP patients, 56 having undergone gingivoperiosteoplasty and 64 not. Using 3-D scans of maxillary models their analysis showed more severe maxillary underdevelopment in patients treated with a gingivoperiosteoplasty technique. This is at odds with the review by Farronato *et al.* (2014) who found that of the studies examining gingivoperiosteoplasty all reported good facial growth results. The review was limited with loose selection criteria and included only articles written in English. However, secondary bone grafting had better outcomes for maxillary growth, with more positive results for intracranial relationships, whilst primary bone grafting had more negative results on the skeletal growth.
Surgical techniques for repair are continually evolving and each method will be practiced differently by each surgeon.

2.4.2 Adverse Effects of Surgical Repair

No matter which technique is used there will always be an element of scarring. The extent and severity of scarring will influence facial and maxillary growth and development. This can lead to functional, cosmetic, and psychological problems (Gundlach and Maus, 2006). Multiple factors lead to typical features of a scar, including location, size, aetiology, suturing technique, suture material, wound care, wound healing, as well as individual age, race, and genetic predisposition (Frans *et al.* 2012). Repair of the orofacial structures results in scarring, which in turn is likely to cause maxillary hypoplasia and explains why the cleft population most commonly (70%) has a class III skeletal relationship (Williams *et al.* 2001). A recent study by Naqvi *et al.* (2015) in India compared 180 unilateral cleft lip/ palate affected individuals using lateral cephalograms, 90 of whom had been operated on and 90

who had received no operative intervention. The operated group showed a statistically significant decrease in maxillary length and SNA angle in all three age groups (3-5 years, 8-10 years and 20-25 years) compared to the unoperated group. They concluded that the maxilla showed normal growth potential in the unoperated group, whereas, "*lip and palate repair results in retarded growth of maxilla, which causes midface deficiency beyond acceptable sagittal limits.*"

The same conclusions were made by Saperstein *et al.* (2012) using a similar method in children aged 6-16 years. They also compared the untreated group to an unaffected control group and found no statistically significant difference in growth.

Re-evaluation of the Sri Lankan Cleft Lip and Palate project data, originally reported in 1990 (Mars *et al.* 1990), found that the adverse effects of unoperated clefts on the growth of the maxilla in patients with UCLP were restricted to the size of the basal maxilla, more so with respect to height than length (Liao and Mars 2005a). This was postulated to be due to both intrinsic anatomical and functional effects. However, in the case of those individuals with a UCLP that had been operated on, it was concluded that repair of the palate inhibited the forward displacement of the basal maxilla and the antero-posterior development of the maxillary dentoalveolus. Whilst the palatal repair had no detrimental effects on the downward displacement of the basal maxilla or on palatal remodelling (Liao and Mars 2005b), repair of the lip was found to have a favourable bone remodelling effect and controlled uprighting of the maxillary alveolus (Liao and Mars 2005c).

Chiu and Liao (2012) attempted to review whether the severity of the initial cleft would impact maxillary growth, and logic would dictate this to be the case. However, the review included just four retrospective, medium to low quality studies and drew no robust conclusions. A study by Johnson *et al.* 2000, not included in the review, reported there was

no evidence the initial cleft area influenced the dental arch relationships per the 5-Year Olds' Index, at age six years.

2.5 The Maxillary Arch

Normal growth and development of the dental arches has been studied for many years, as has the effect of orthodontic treatment on maxillary growth. Bishara *et al.* (1997) assessed arch width changes in patients from 6 months to 45 years of age by measuring the intercanine (between cusp tips) and the intermolar widths from study models as shown in Figure 3.

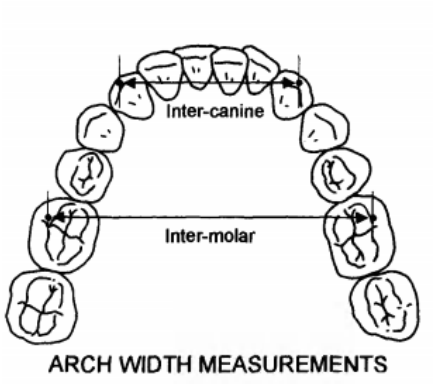

Figure 3. Measurements of arch widths in post eruption stages. (Bishara *et al.* 1997, p403).

Between the ages of 3 and 5 years, the mesial cusp tips of the second deciduous molars were used for measurement, but once the first permanent molars had erupted the mesiobuccal cusps of these teeth were used instead. They found that the mean values for maxillary intermolar width, using the second deciduous molars, were 43.5mm and 40.8mm for males and females respectively. The maxillary intercanine widths were 30.3mm and 28.4mm for males and female respectively.

Dental arch shape or form has been described since the advent of orthodontics, and whilst numerous descriptors exist, no single one is universally accepted. There are some basic archforms: Bonwill-Hawley, Catenary Curve and Trifocal ellipse or Brader. However, these may not conform to every patient and instead, a more general description of arch form is often used and these are shown in Figure 4, namely: 'U shaped', 'V shaped', 'square' or 'omega'.

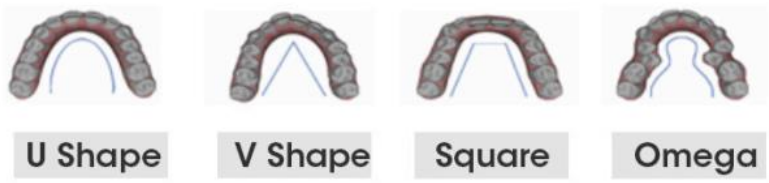

Figure 4. Images of arch shape. (colgateoralhealthnetwork.com)

2.5.1 Maxillary Arch Measurements – Digital Analysis

Prior to the digital age, measurements from study models would have been acquired using analogue dial calipers (Bishara *et al. 1997),* potentially introducing significant measurement errors. Digital calipers improved on this, but with the advent of laser scanned study models, (Wojtaszek-Slominska *et al.* 2010) the potential for a fully digitised system of measurement is now possible. Direct intra-oral scanning, although not commonly available as yet, has the potential to further reduce errors by removing the impression stage of image acquisition (Rajshekar *et al.* 2017).

The reliability of measurements from on screen digital models, versus measurements from conventional plaster models using digital calipers has been investigated by Lemos *et al.* (2015). They considered a 0.2mm difference to be clinically significant for their study. The

same examiner took three sets of all the measurements using both techniques and they found no statistically significant differences except for the overjet measurement. Overall, they considered digital model analysis to be a reliable alternative to examining cast dental models. A systematic review by Fleming *et al.* (2011) comparing measurements gained from scanned digital study models versus plaster casts also recommended the use of scanned digital models as an alternative to using conventional plaster models and hand held calipers.

2.5.2. The Cleft Maxillary Arch

In determining the success of surgical repair of the cleft, maxillary models are one method of assessment. Investigation of these models will provide data that could account for improvements in surgical outcomes, between CSAG and CCUK.

Arch shapes associated with cleft have also been studied along with changes over time. Mazaheri *et al.* (1971) used a photocopy method to assess changes in arch shape over time of 30 people with cleft lip / palate, 40 with cleft palate and an equal number of people without cleft. At 5 years of age the upper posterior arch width and inter-canine width were reduced in the CLP group compared to the unaffected participants, and in general for all cleft affected individuals a decrease in maxillary width was more evident than a decrease in length. However, the accuracy of the method employed in this study must be called into question. For instance, if the occlusal surfaces of the teeth on the plaster model are not in a single well defined plane, but are instead on a curve e.g. Curve of Monson or Spee, the teeth will not lay flush to the scanning surface of the photocopier. This means that some of the teeth will inevitably be out of focus on the final image, making landmark identification less accurate and reliable. In addition, the best fit line of the arch line appears subjective to the assessor rather than mathematically determined.

More recently, scanned maxillary arch models were used in a study by Wojtaszek-Slominska *et al.* (2010) with accuracy reported between 0.01mm and 0.5mm. The images in Figure 5 show the reference points used to obtain measurements of anterior and posterior arch widths (Cr-Cl, Er- El), arch length (L), inclination of major (*l*) and lesser (*i*) segments, radius of major and lesser segments, anterior palatal depth (Ad) and posterior palatal (Pd) depth.

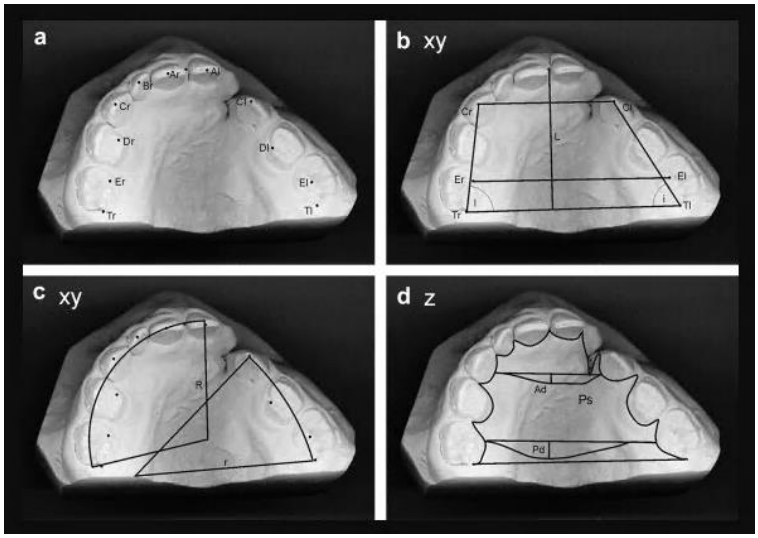

Figure 5. Study models: reference points and measurements used in the analysis.

(Wojtaszek-Slominska *et al.* 2010. P 157)

The authors argued that occlusal model analysis is superior to assessment by cephalometry due to rotation errors, which increase or decrease the expression of a dimension, tracing errors and unnecessary X-ray exposure. Likewise, they disparage the Goslon scoring method, as it is good for screening, but does not indicate the anatomical nature of the maxillary derangement.

Further to this, Generali *et al.* (2017) published a paper evaluating the maxillary arch and palate of UCLP affected individuals. Figure 6 shows the evaluation of intercanine and

intermolar widths, and the palatal surface area and volume under a designated occlusal plane. Nineteen nine-year-old UCLP affected individuals were matched to nineteen non-cleft controls.

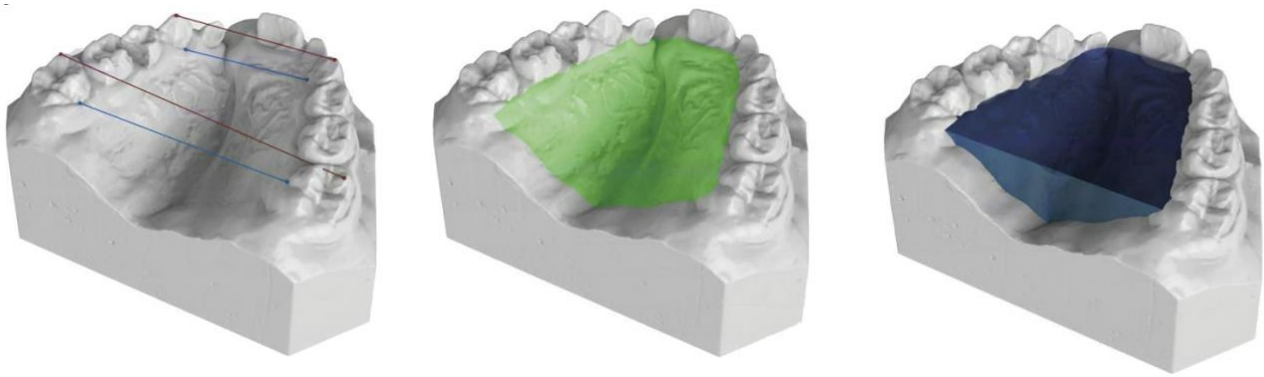

Figure 6. Digital models showing linear measurements, palatal volume and palatal area. (Generali *et al.* 2017 p. 642-643)

They found that the intercanine width, palatal area and palatal volume were all significantly smaller in the UCLP group compared to the control group, but there was no significant difference in intermolar width. The discussion within this paper considers the potential adverse effects of having a smaller palatal volume with respect to space for the tongue. They describe how limitation of this space may result in an anterior open bite, mouth breathing, backwards growth rotations, and a low tongue position increasing the mandibular intermolar width and resulting in crossbites. Therefore, their conclusion was that expansion of the maxillary arch may be beneficial in UCLP patients. Limitations of this

study include a relatively small sample size, missing primary teeth meaning that some data were missing, and a sample which only included males.

Similar findings with respect to arch width and palatal depth have also been reported by Šmahel *et al.* (2004) and Rusková *et al.* (2014). Both also found that the depth of the anterior palate was greatest on the cleft side, whereas the maximum depth posteriorly was at the midline or the non-cleft side. Moreover, the palate had a greater incline on the cleft side and there was greater variability in the shape of the palate of ULCP patients (Ruskova *et al.* 2014). Smahel *et al.* (2004) also concluded that the reduced width and depth of the palate substantially reduced the space for the tongue in their study, which compared UCLP affected boys with a matched control group.

A further study by Mishima *et al.* (1996) utilised the canine points, tuberosity points and the incisal point on infant ULCP maxillary models to deduce linear and angular measurements (Figure 7).

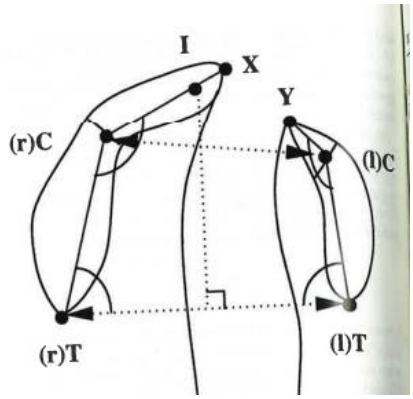

Figure 7. Diagram showing the reference points, linear and angular measurements constructed on the infant UCLP maxillary model. (Mishima *et al.* 1996. p314)

A systematic review and meta-analysis that examined the effectiveness of presugical infant orthopaedic treatment for cleft lip and palate patients (Papadopoulos *et al.* 2012), found a small but significant difference where the angle between the midpoint of the tuberosities, tuberosity and canine cusp was used as an outcome measure.

Using maxillary models allows for both transverse and anteroposterior arch assessments, rather than just an antero-posterior assessment as is the case with cephalometrics. More recently, digital scanning methods of assessment have been shown to be as accurate as traditional analogue / part digital techniques (Fleming *et al.* 2011). Having access to the quantitative raw data obtained from such digital models, rather than potentially subjective analogue or part-digital techniques, should improve the understanding of cleft and its treatment on arch form.

2.6 The Research Question

Since the recommendations put forward by CSAG 1998 have been adopted by the cleft community, training, caseload and cleft team composition have undergone significant change. The improvements in cleft outcomes have been well documented by the subsequent CCUK study (Al-Ghatam *et al.* 2015, Smallridge *et al.* 2015, Sell *et al.* 2015, Waylen *et al.* 2015). Whilst the changes in dentoalveolar relationships have been assessed, by the somewhat subjective 5-Year Olds' Index, the transverse dimensional changes are less well reported. The specific research question of the current project was therefore: Following the reorganisation and centralisation of cleft services in the UK, has there been an improvement in maxillary arch transverse dimensions?

2.7 Aim and Objectives

The aim of the research was:

- To determine if the transverse dimensions of maxillary unilateral cleft lip and palate affected children has improved since the implementation of the CSAG recommendations?

The objectives of the research were:

1. Deduce the quantitative differences in the intermolar width, intercanine width and the distance to the midline for each of the canines and second deciduous molars between the two populations, CSAG and CCUK.
2. Deduce the quantitative differences in the anterior depth and posterior depth and arch length between the two populations, CSAG and CCUK.

3. Deduce the quantitative differences in arch form angles between the two populations, CSAG and CCUK.
4. Where possible compare these to existing data of children of a normal population.

3 MATERIALS AND METHODS

This study was limited to the investigation of unilateral cleft lip and palate (UCLP) children at the age of 5 years. Clefts of this type reflect the problems seen in all cleft forms, and provide a relatively unaffected side for comparison. The 5-year-old age group have models available from both the CSAG and CCUK studies.

3.1 Permissions

The current project was considered by the Research and Ethics Departments at the University of Bristol and University Hospitals Bristol NHS Foundation Trust and was considered to be a service evaluation. It was also considered by the Audit Steering Committee of University Hospitals NHS Foundation Bristol and accepted and registered as service evaluation audit (SE:180 (Appendix 2)).

The materials used in this study were maxillary models of 5-year-olds from the previously reported CSAG (Sandy *et al.* 2001) and CCUK (Persson *et al.* 2015) studies. The original CSAG study was also considered to be an audit project, which did not require research ethics committee approval. Permission was sought and granted from the CCUK study team at University Hospitals Bristol NHS Foundation Trust, to gain access to the CCUK models (Appendix 1).

3.2 Materials

1. 5-year-old maxillary models from the CSAG study (number = 114)
2. 5-year-old maxillary models from the CCUK study (number = 175)
3. 3 Shape R700™ Orthodontic Scanner – 3Shape HQ, 3Shape A/S, Holmens Kanal 7, 1060 Copenhagen, Denmark
4. OrthoAnalyzer™ software – ESM Digital Solutions, ESM Digital Solutions Ltd., Unit 4, Broadmeadow Hall, Applewood, Swords, Co. Dublin, K67 Y5F2, Ireland
5. Microsoft Excel™ – Microsoft Corporation, Redmond, WA, USA
6. Stata – StataCorp 2019. *Stata Statistical Software: Release 16.* College Station, TX: StataCorp LLC.

3.3 Methods

Maxillary models from both the CSAG and CCUK studies were identified and inventoried. All of the models were previously anonymised of any patient information and instead given a unique identifier code. This was used as the label in the OrthoAnalyzer™ software program once scanned.

All the model scanning was completed by a single researcher (CM), with the models being digitally scanned in a random order using the 3 Shape R700™ laser scanner. The scanner was calibrated weekly to ensure a 0.02mm degree of accuracy as per the manufacturer's instructions. Although the same instructions state that it is necessary to perform a recalibration of the machine following any significant ambient temperature fluctuation, this did not occur, so no such recalibration was necessary in the current study.

Once all the models were scanned, a dental technician allocated a random number code to the models using a random number generator (https://www.randomcodegenerator.com/en/generate-codes), which anonymised the model to its group (either CSAG or CCUK). This allowed the researcher CM to measure all the models using the OrthoAnalyzer™ program, blinded as to which group each model belonged.

All of the initial measurements were undertaken over a one month period at various sittings. The measurement values were saved on the OrthoAnalyzer™ program and transferred onto a Microsoft Excel™ spreadsheet at the time of measurement.

Measurements obtained included:

1. Anterior width – cusp tip of URC to cusp tip of ULC (*C-C).*
2. Posterior width – mesiobuccal cusp of URE to mesiobuccal cusp of ULE (*E-E*).
3. Anterior depth – vertical perpendicular distance between the midpoint of *C-C* line and the palate*.*
4. Posterior depth – vertical perpendicular distance between the midpoint of *E-E* line and the palate*.*
5. Arch length– mesial incisal edge of the upper central incisor (non-cleft side) to line constructed distal to Es
6. Affected side – distance from the constructed midline to the affected side canine tip and affected side mesiobuccal cusp of the E.
7. Non-affected side – distance from the constructed midline to the non-affected side canine tip and non-affected side mesiobuccal cusp of the E
8. Angle created between the intermolar width line and canine for each side.

If any of the features required to gain a single measurement were not present, this measurement was not recorded for that model. All measurements were completed by a single researcher (CM).

For all measurements OrthoAnalyzer™ software was used. This involved the creation of an occlusal plane (Figure 8), which used the lowest point on the palatal gingival margin of the upper Es and upper central incisor of the non-affected side.

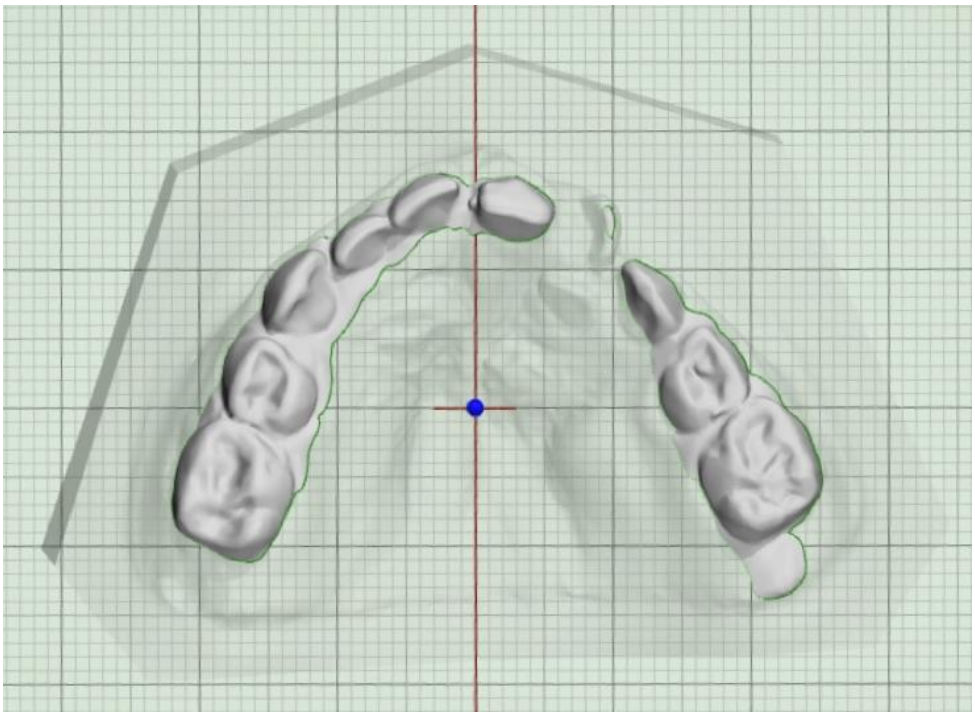

Figure 8. Image to show creation of the occlusal plane in OrthoAnalyzer™.

If any of these reference points were not present on the model, then an occlusal plane could not be established. This software includes functions which allow linear measurements, distance to plane measurements and angular measurements.

Linear measurements, as depicted in Figure 9, were completed from the cusp tips of the upper right primary canine to the upper left primary canine (inter canine width), and from mesiobuccal cusp tip of the upper right second primary molar to upper left second primary molar (inter molar width). The arch length was determined as the linear distance from the mesio-incisal corner of the central incisor on the non-affected side to a disto-palatal line drawn between the distal surface of the upper primary second molars (Figure 9). The occlusal plane was rotated to create a 90^{o} angle between these two lines.

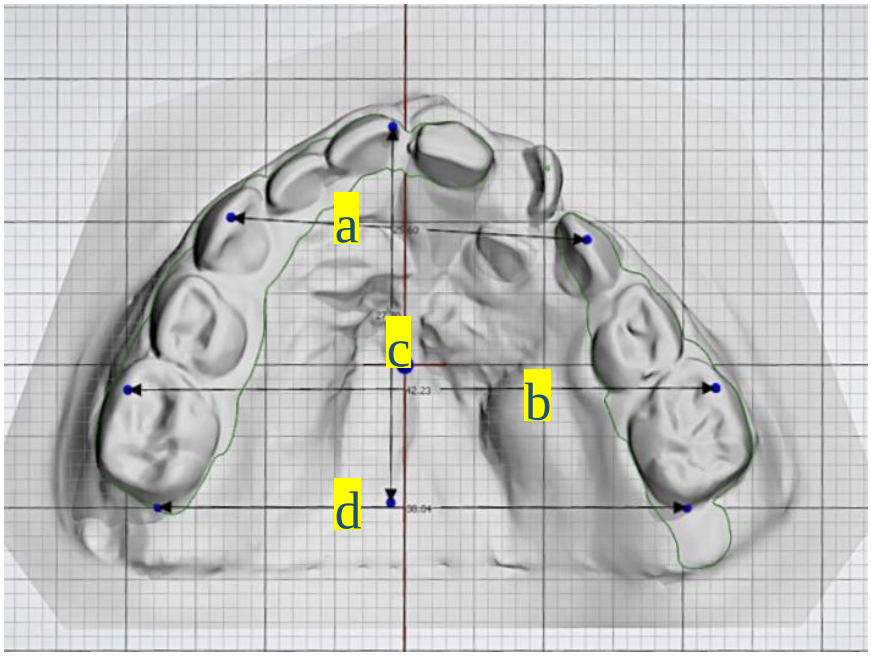

Figure 9. Image to show linear measurements; a) intercanine width. b) intermolar width. c) arch length which is perpendicular to the d) disto-palatal line.

The anterior and posterior depths, shown in Figure 10, were measured with a vertical perpendicular from the occlusal plane at the midpoint of the inter canine or intermolar width to the palate. To enable independent measurements of the affected and non-affected sides a sagittal plane was constructed as depicted in Figure 11, indicative of the midline. This sagittal plane was established through the contact point of the two central

incisors, or where these were not present the midpoint of the incisive papilla.

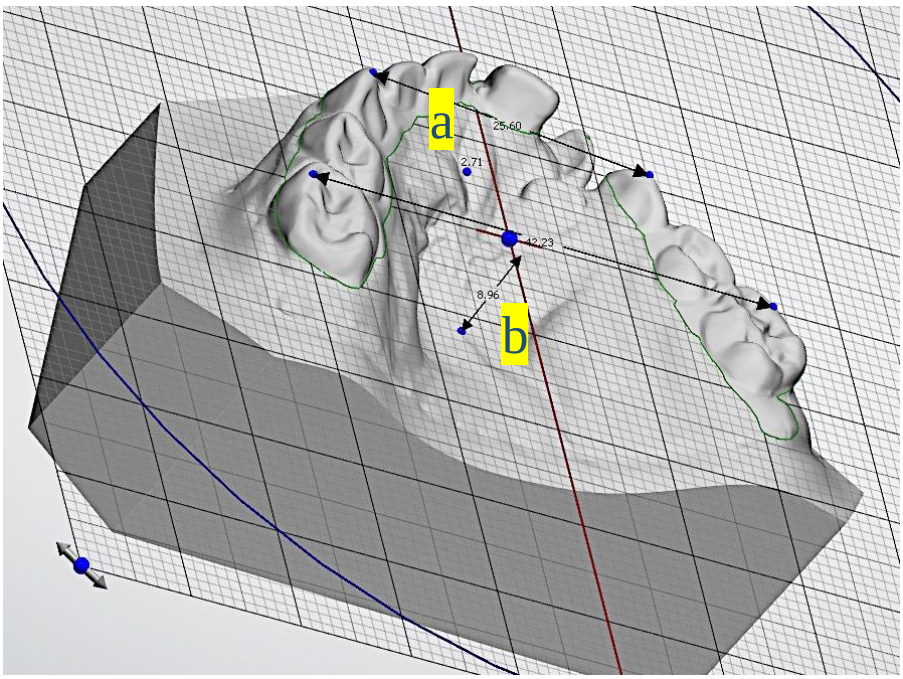

Figure 10. Image to show vertical depth measurement from the constructed occlusal plane to the depth of the a) anterior depth and b) posterior depth.

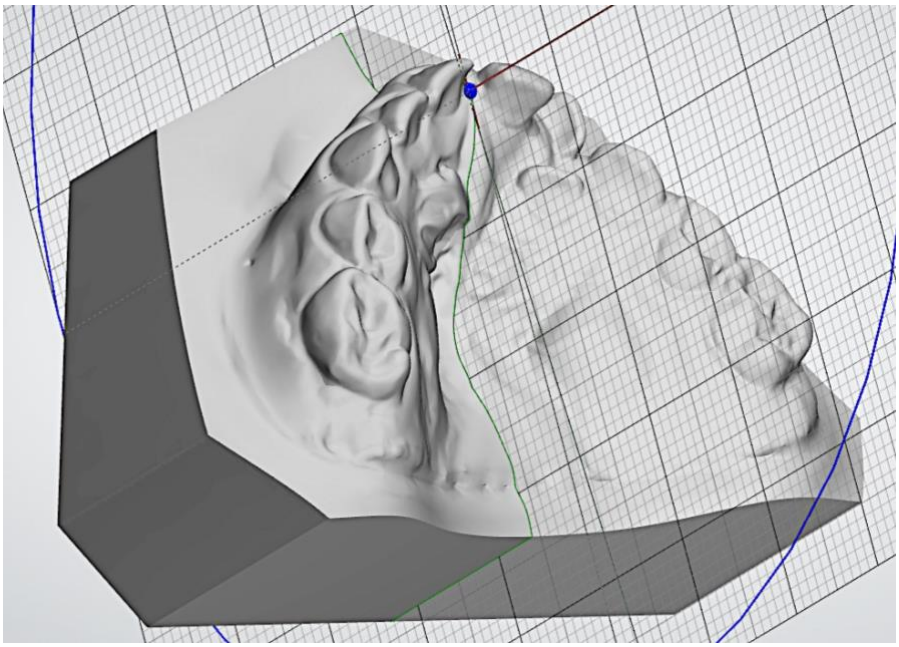

Figure 11. Image to show creation of sagittal plane.

Where neither were clear, as was the case with 15 of the models, these were assessed independently by a second researcher (AI), discussed and a consensus reached. The model was then rotated so that the sagittal plane was perpendicular to the line previously constructed distal to the Es. The affected and non-affected side measurements from the canines and second primary molars could then be found using the originally identified canine tip and mesiobuccal cusp of the E to the sagittal plane as shown in Figure 12.

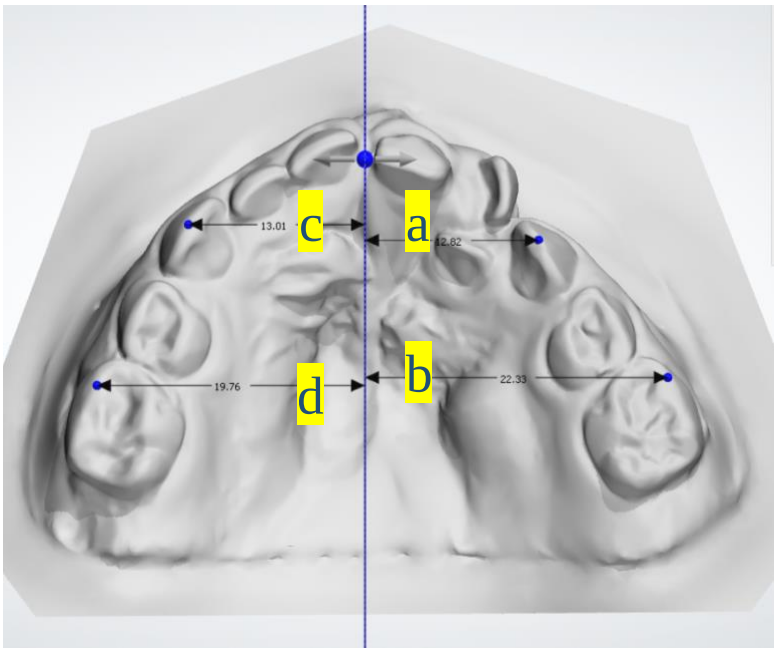

Figure 12. Image to show linear measurements to the sagittal plane midline. a) affected side canine to midline. b) affected side E to midline. c) non-affected side canine to midline. d) non-affected side E to midline.

Measurement of the angle was determined using the angle function in OrthoAnalyzer™. The angle was created on both the affected and non-affected sides between the canine tip, ipsilateral mesiobuccal cusp of the E and the contralateral mesiobuccal cusp of E, as illustrated in Figure 13.

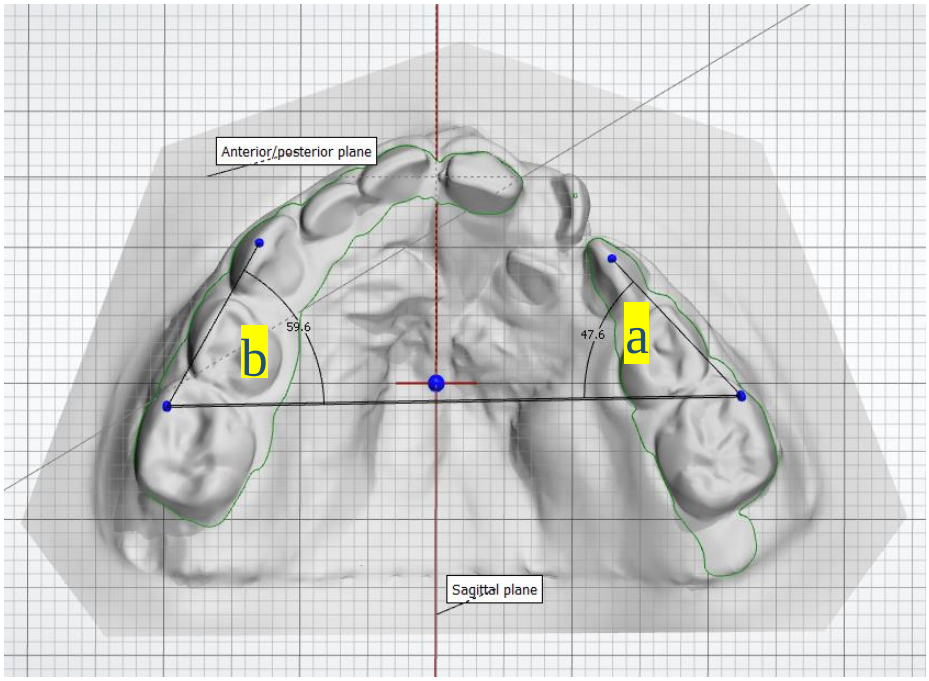

Figure 13. Image showing angular measurements. a) affected side angle. b) non-affected side angle.

All measurements were recorded in a Microsoft Excel™ spreadsheet.

3.4 Reproducibility

A random selection of 15 models from each of the two cohorts was provided to CM by the same dental technician who allocated the original model codes. The technician deleted any previous measurements within the software prior to re-measurement. The 30 models were then re-measured by CM a minimum of two weeks following the initial measurements. This allowed for agreement statistics to be calculated.

3.4.1 Data Analysis

The data were analysed using Stata version 16 (Stata Corp, College Station, Texas, USA) statistics package, with a predetermined significance level of $\alpha = 0.05$ in accordance with the null hypotheses:

1. There are no significant difference in any of the linear or angular measurements between the CSAG and CCUK cohorts

Reproducibility was tested using both Lin's Concordance (Lin 1989, 2000) and Intraclass correlation coefficients (3,1).

When comparing the cohorts CSAG and CCUK, the data on the linear and angular measurements of the models are presented as means, standard deviations and 95% confidence intervals of the means, and differences explored using two sample t-tests, the result of this expressed as a probability. This method assumes independent samples, equal variance and that the data follow a normal distribution.

When comparing sides and taking the cohort into consideration the data were restructured into a form suitable for a linear mixed model analysis. Margin plots were constructed and illustrate the interaction between the cohort with the affected and non-affected side.

When comparing the affected and non-affected sides, irrespective of cohort, the linear and angular measurements of the models are presented as means, standard deviations and 95% confidence intervals of the means, and the differences explored using two sample t-tests expressed as a probability.

4 RESULTS

4.1 Agreement Analysis

The repeatability of the measurements undertaken on the 30 models (15 from each cohort), re-measured by the same researcher (CM), were tested using both Lin's concordance correlation coefficient and interclass correlation coefficient (3,1). Lin's concordance correlation coefficient combines measures of both precision and accuracy on how far the observed data are from the line of perfect concordance. Table 4 shows the Lin's values for each of the measurements, and Figures 14 and 15 illustrate the best and worst plots from this analysis.

Measurement	**Agreement**
Intercanine width	0.994
Affected side C	0.969
Non-affected side C	0.808
Anterior depth	0.960
Intermolar width	0.991
Affected side E	0.962
Non-affected side E	0.915
Posterior depth	0.996
Arch Length	0.991
Affected side angle	0.979
Non-affected side angle	0.966

Table 4. Lin's concordance correlation coefficient values for each measurement.

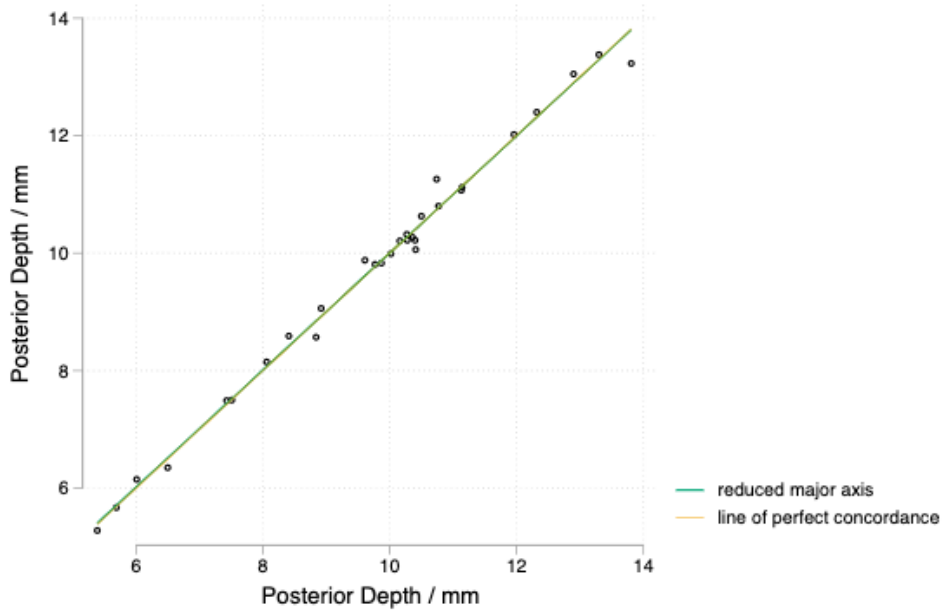

Figure 14. Lin's concordance correlation coefficient for measurement of posterior depth. The line of perfect concordance (orange) and line of best fit or reduced major axis through the data points (green) are coincident. There is little scatter in the data points.

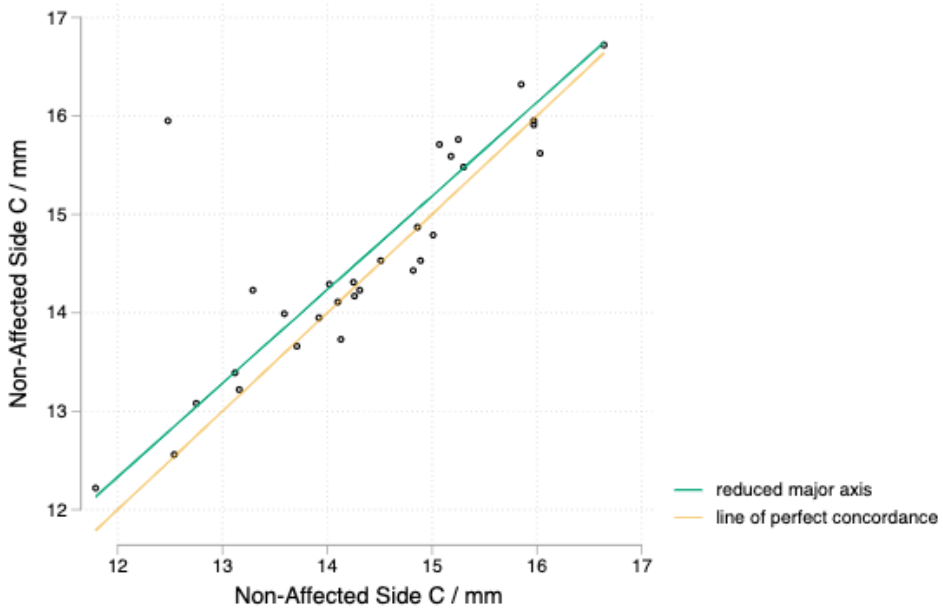

Figure 15. Lin's concordance correlation coefficient for measurement of non-affected side C. The line of perfect concordance (orange) and line of best fit or reduced major axis through the data points (green) are not coincident. There is greater scatter in the data points.

The Interclass Correlation Coefficient (3,1) findings are presented in Table 5. The (3,1) refers to 'model 3' where each subject is assessed by each rater, but the raters are the only raters of interest. The term 'form 1' refers to the reliability calculated on measurements by a single rater. This is applicable to our study as each model is randomly selected from all possible models, and is measured by the same set of observers, with these observers being the only ones of interest.

4.2 Intraclass Correlation Coefficient (3,1)

Measurement	**Agreement (ICC 3,1)**	**95% CI**
Intercanine width	0.994	0.987 to 0.997
Affected side C	0.973	0.944 to 0.987
Non-affected side C	0.822	0.660 to 0.911
Anterior depth	0.969	0.936 to 0.985
Intermolar width	0.992	0.983 to 0.996
Affected side E	0.963	0.923 to 0.982
Non-affected side E	0.916	0.830 to 0.959
Posterior depth	0.996	0.991 to 0.998
Arch Length	0.991	0.982 to 0.996
Affected side angle	0.981	0.960 to 0.991
Non-affected side angle	0.971	0.938 to 0.986

Table 5. Table showing the intraclass correlation coefficients (3,1) and 95% confidence intervals for each of the measurements.

The ICC (3,1) shows good agreement, with values over 0.95 and narrow 95% confidence intervals for all measurements except for the non-affected side C (0.822; 0.660 to 0.911) and non-affected side E (0.916; 0.830 to 0.959) measurements.

4.3 Analysis of Cohorts

There were a number of models where certain measurements could not be undertaken because of missing or severely worn teeth, as listed in Table 6. In eight of the models none of the measurements could be completed. Of these four were from CSAG and four from CCUK

Measurement	**CSAG (114)**	**CCUK (175)**
Intercanine width	9 (7.8%)	10 (5.7%)
Affected side C	14 (12%)	14 (8%)
Non-affected side C	14 (12%)	13 (7.4%)
Anterior depth	15 (12.9)	19 (10.8%)
Intermolar width	7 (6%)	9 (5.1%)
Affected side E	12 (10.3 %)	10 (5.7%)
Non-affected side E	12 (10.3%)	10 (5.7%)
Posterior depth	13 (11.2%)	13 (7.4%)
Arch Length	14 (12%)	13 (7.4%)
Affected side angle	14 (12%)	14 (8%)
Non-affected side angle	13 (11.2%)	13 (7.4%)
No measurements possible	4 (3.4%)	4 (2.3%)

Table 6. The number and percentage of models from each of the two cohorts (CSAG and CCUK) where specific measurements were not possible.

The following plots and tables (Figures 16 to 26 and Tables 7 to 17) illustrate the differences between each measurement for the two cohorts CSAG and CCUK. The plots allow visualisation of the means, associated 95% confidence intervals and the cumulative data distribution for each measurement in each cohort. The calculated p value is a probability from the two-sample t-test comparing the two sample means for each measurement.

Anterior Segment - Anterior Width Measurement

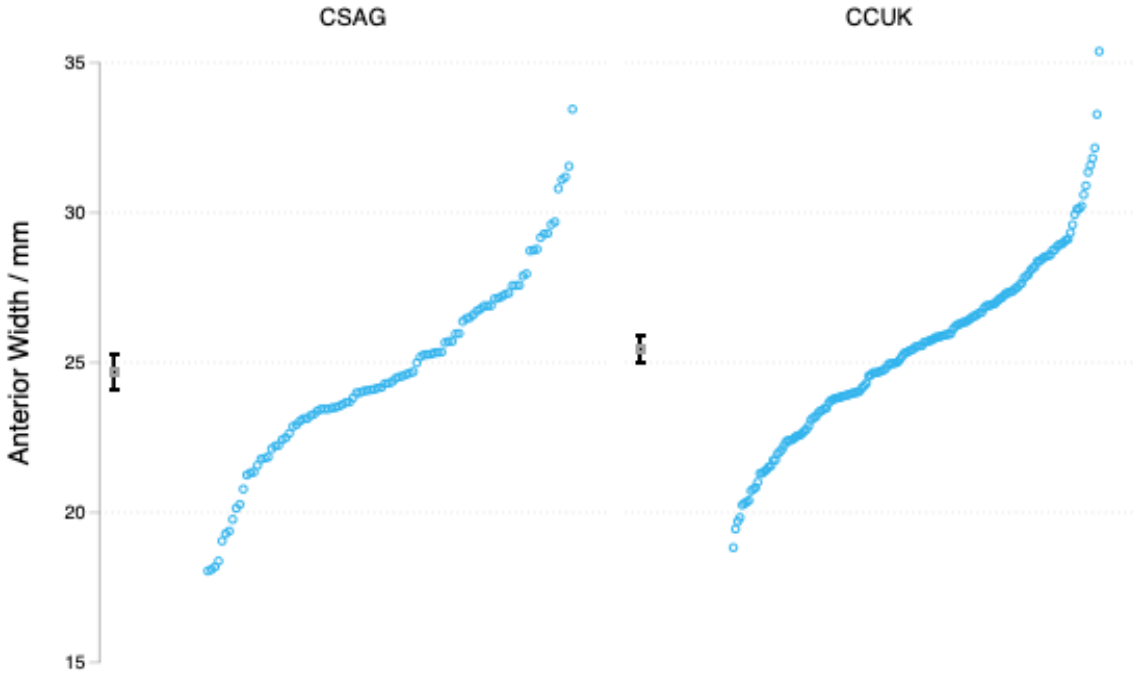

Figure 16. Graph showing the distribution, means and 95% confidence intervals of the mean for the CSAG and CCUK anterior width measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	104	24.69	3.12	24.08 to 25.29	0.044
CCUK	166	25.45	2.96	25.00 to 25.91	

Table 7. Table showing the cohort numbers, means, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for anterior width, along with the estimated p-value.

The data from both cohorts shows a similar distribution and although statistically significantly different (p=0.44), the difference between the means was less than 1mm.

Anterior Depth Measurement

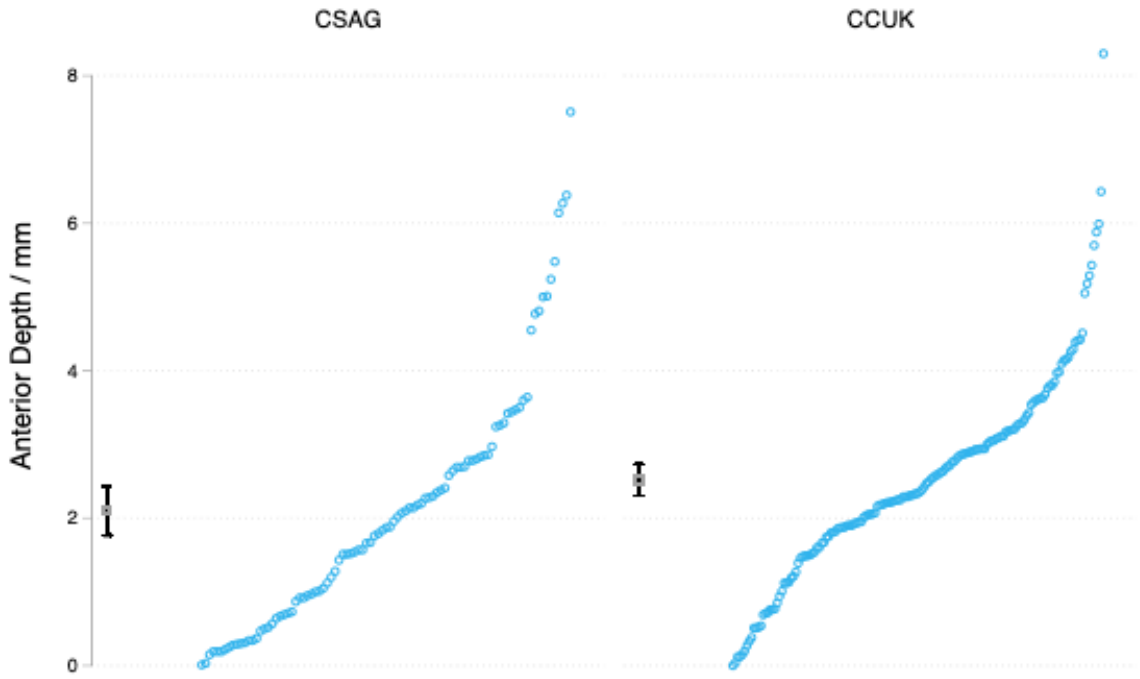

Figure 17. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts anterior depth measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	95	2.10	1.63	1.77 to 2.43	0.029
CCUK	160	2.52	1.36	2.30 to 2.73	

Table 8. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for anterior depth, along with the estimated p-value.

Although the data distribution of the two cohorts were dissimilar, there was a statistically significant difference the mean value (p=0.029), and again it was smaller in the case of the CSAG cohort. The difference between the means was less than 1mm.

Affected Side C Measurement

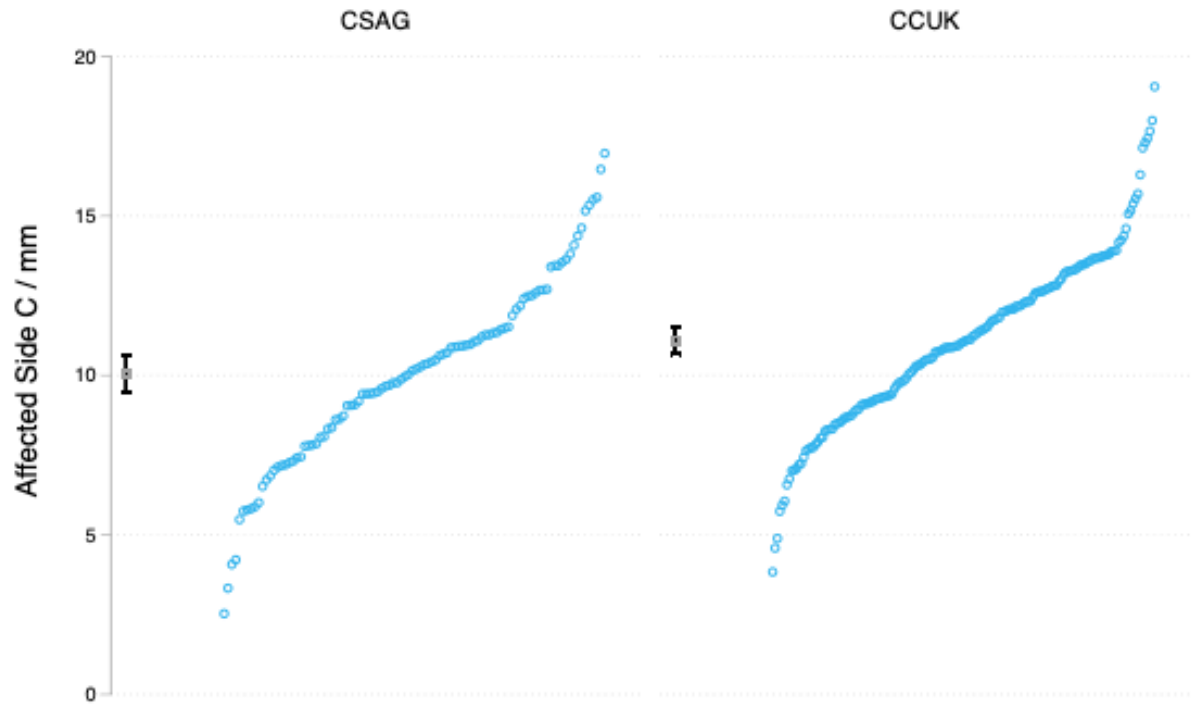

Figure 18. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts affected side C measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	100	10.05	2.90	9.48 to 10.63	0.004
CCUK	161	11.09	2.75	10.66 to 11.52	

Table 9. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the affected side C, along with the estimated p-value.

For the affected side C measurement, the data from both cohorts shows a similar distribution. Once again although statistically significantly different (p=0.004), the measured difference between the means was less than 1mm.

Non-affected Side C Measurement

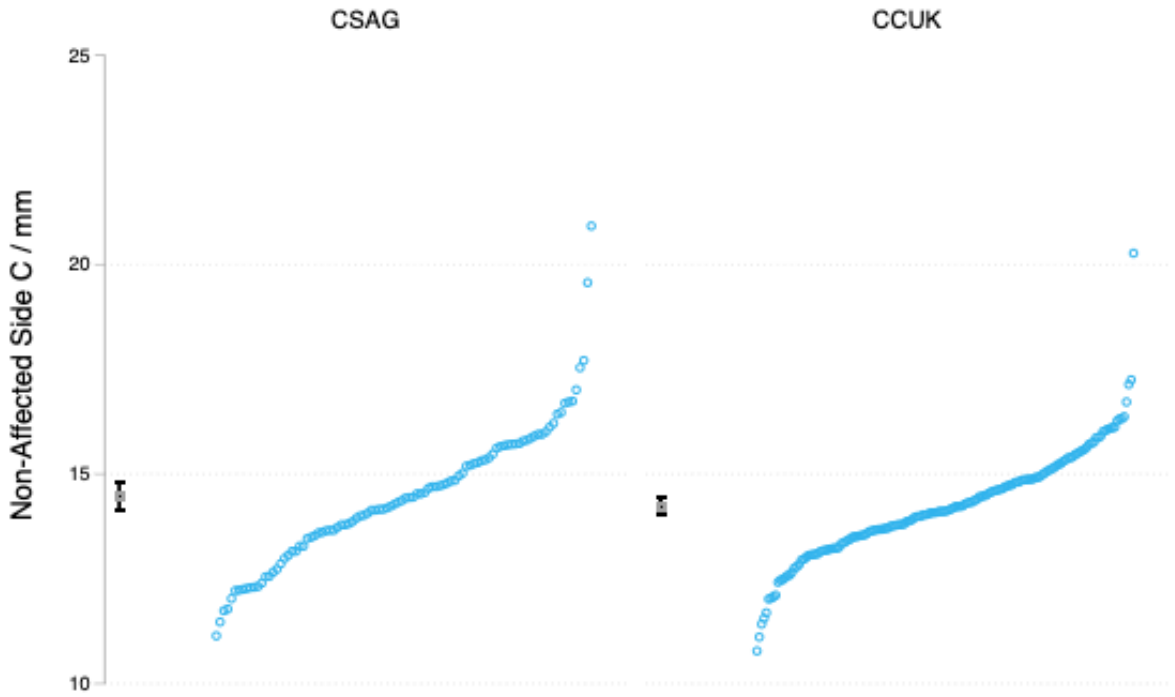

Figure 19. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts non-affected side C measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	100	14.47	1.65	14.14 to 14.80	0.184
CCUK	162	14.23	1.28	14.03 to 14.43	

Table 10. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the non-affected side C, along with the estimated p value.

For the non-affected side C measurement, the data from the two cohorts shows a similar distribution. There was also no statistically significant difference, with the difference between the means being 0.24mm.

Posterior Segment - Posterior Width Measurement

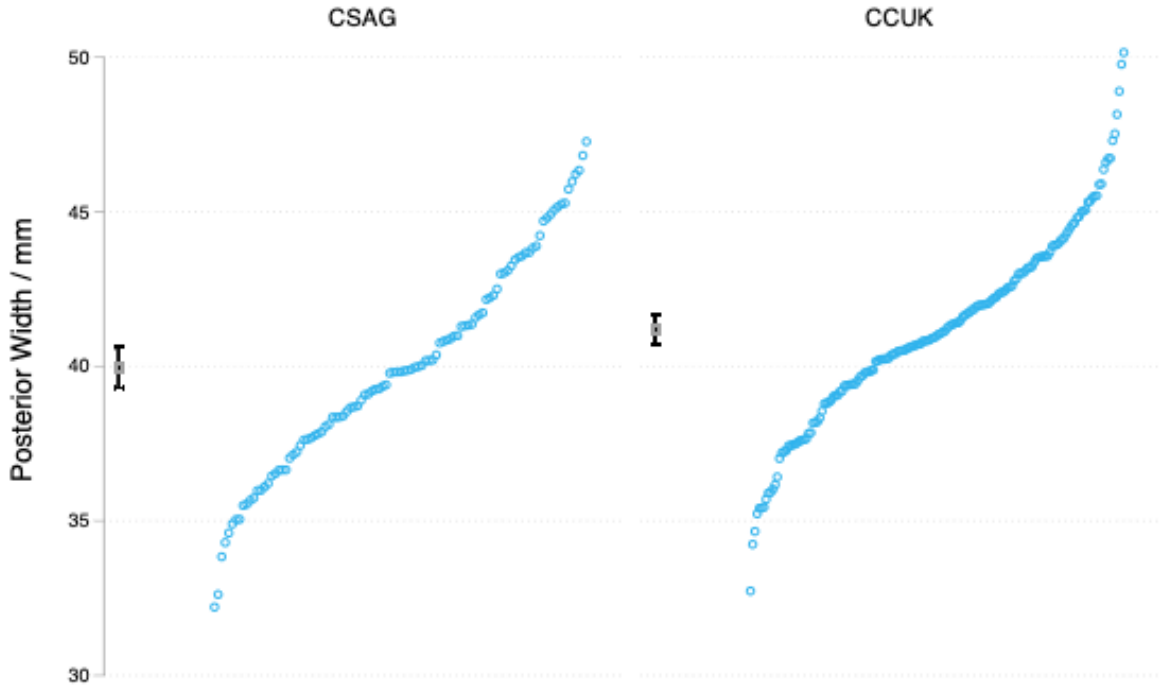

Figure 20. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts posterior width measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	104	39.96	3.39	39.30 to 40.61	0.003
CCUK	166	41.19	3.15	40.71 to 41.67	

Table 11. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the intermolar width, along with the estimated p value.

The data for posterior segment - intermolar width measurement for both cohorts once again shows a similar distribution. There was a statistically significant difference between the two, with the mean value being smaller in the CSAG cohort compared to the CCUK cohort by 1.23mm.

Posterior Depth Measurement

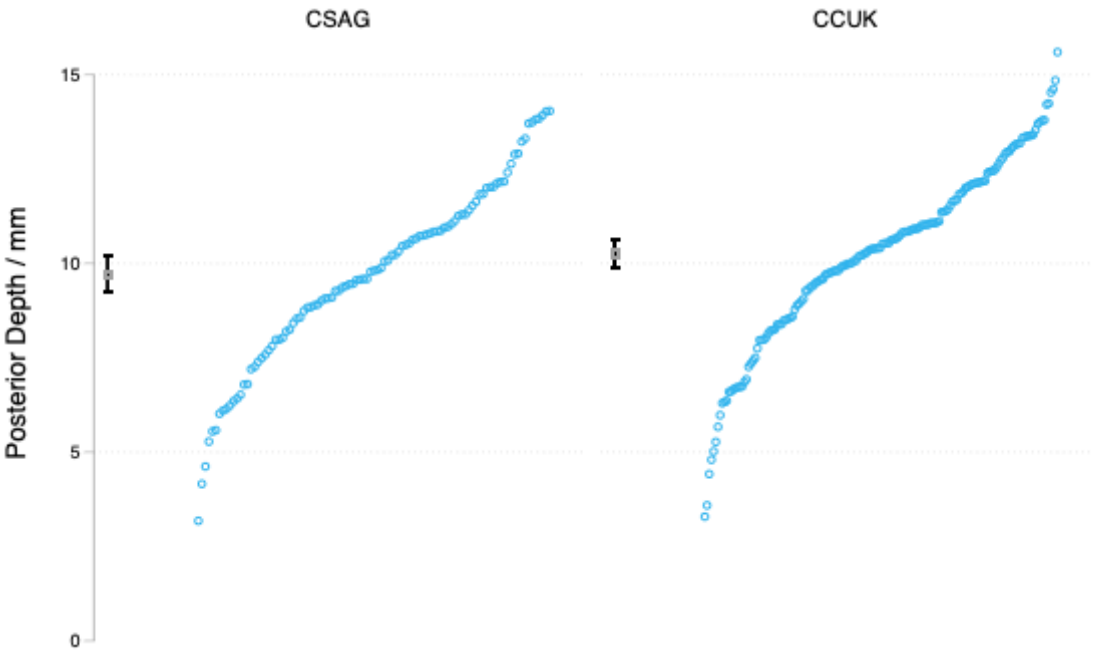

Figure 21. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts posterior depth measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	101	9.71	2.40	9.24 to 10.19	0.073
CCUK	162	10.26	2.41	9.89 to 10.64	

Table 12. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the posterior depth, along with the estimated p value.

In the case of the posterior depth measurement, although the data from the cohorts shows a slightly dissimilar distribution, there was no statistically significant difference between the two groups. The difference between the means was 0.55mm and once again the measurement was slightly smaller in the CSAG cohort

Affected Side E Measurement

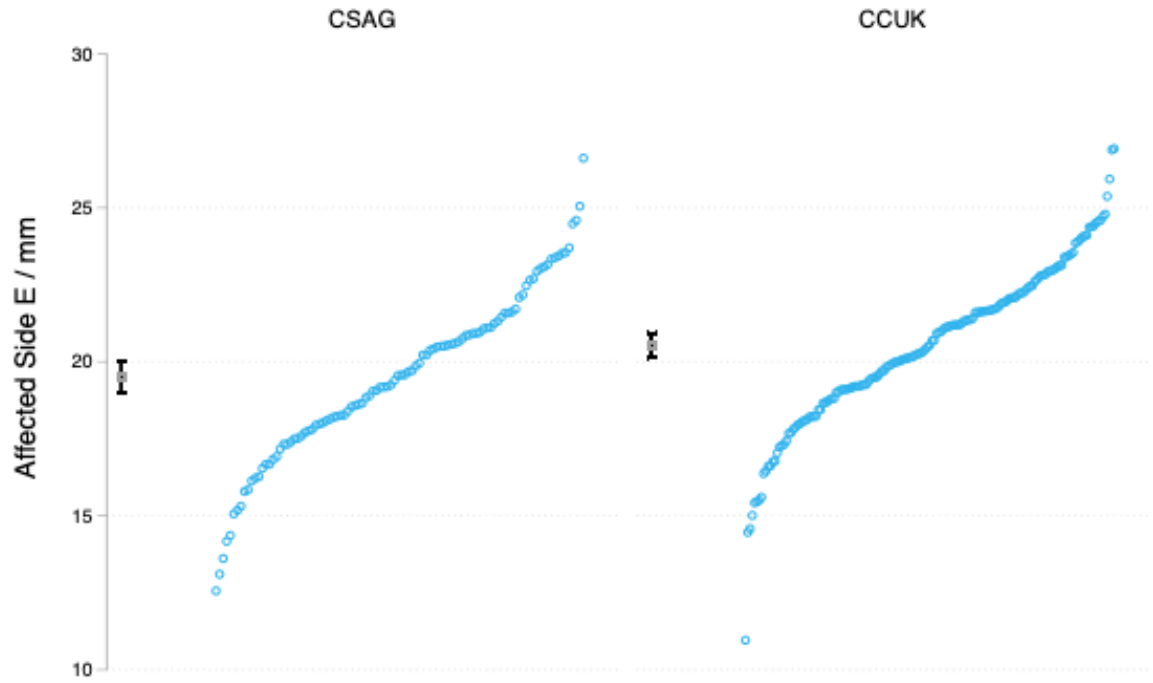

Figure 22. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts affected side E measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	104	19.50	2.74	18.97 to 20.04	0.002
CCUK	163	20.53	2.61	20.12 to 20.93	

Table 13. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the affected side E, along with the estimated p value.

For the affected side E measurement, the data from both cohorts shows a similar distribution. There was a statistically significant difference between the means of 1.03mm, being smaller in the CSAG cohort.

Non-Affected Side E Measurement

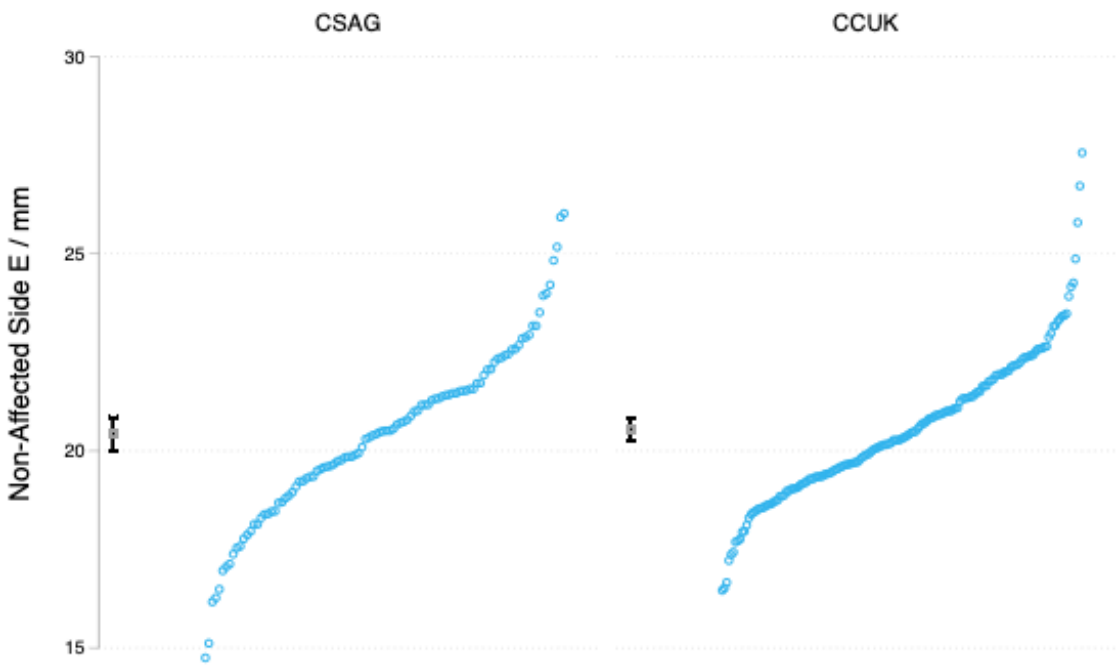

Figure 23. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts non-affected side E measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	104	20.42	2.20	20.00 to 20.85	0.599
CCUK	163	20.56	1.87	20.26 to 20.85	

Table 14. Table showing the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the non-affected side E, along with the estimated p value.

With the non-affected side E measurement the data from both cohorts shows a similar distribution. The difference between the mean values, although smaller in the CSAG cohort by 0.14mm, were not statistically significant different.

Arch Length Measurement

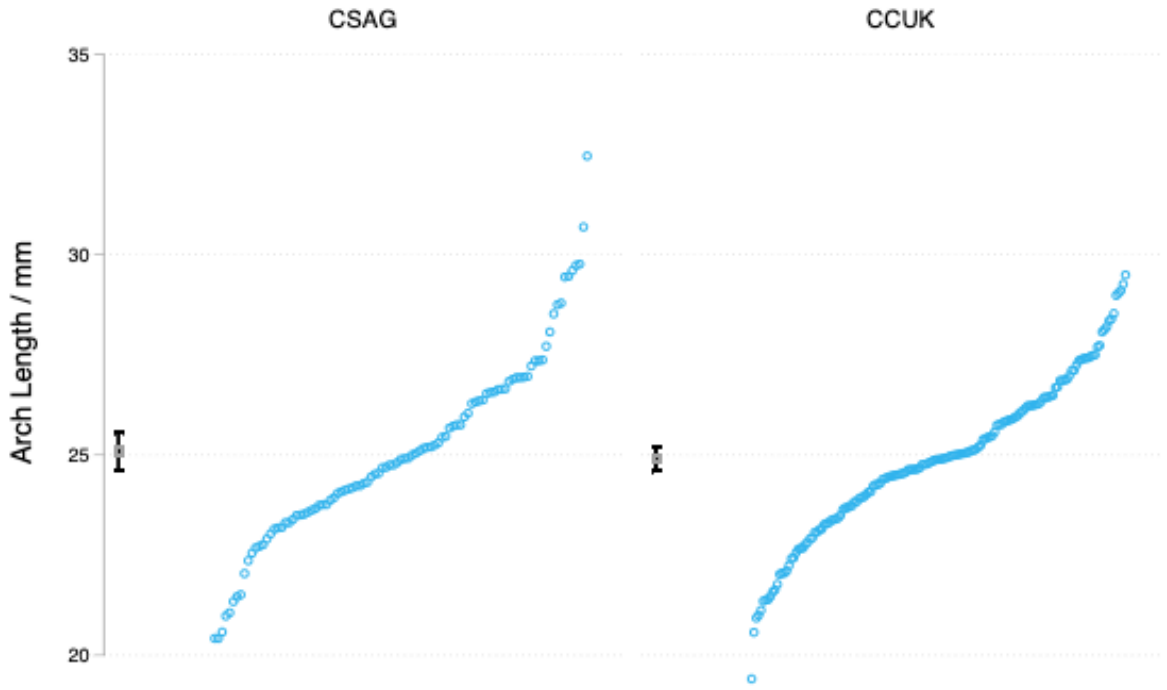

Figure 24. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts arch length measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	101	25.09	2.33	24.63 to 25.55	0.485
CCUK	161	24.90	1.97	24.59 to 25.21	

Table 15. Table to display the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the arch length, along with the estimated p value.

For arch length measurement, the data from both cohorts shows a similar distribution. For this measurement the mean value was smaller in the case of the CCUK cohort. This difference was very small at 0.19mm, which was not statistically significant.

Affected Side Angle Measurement

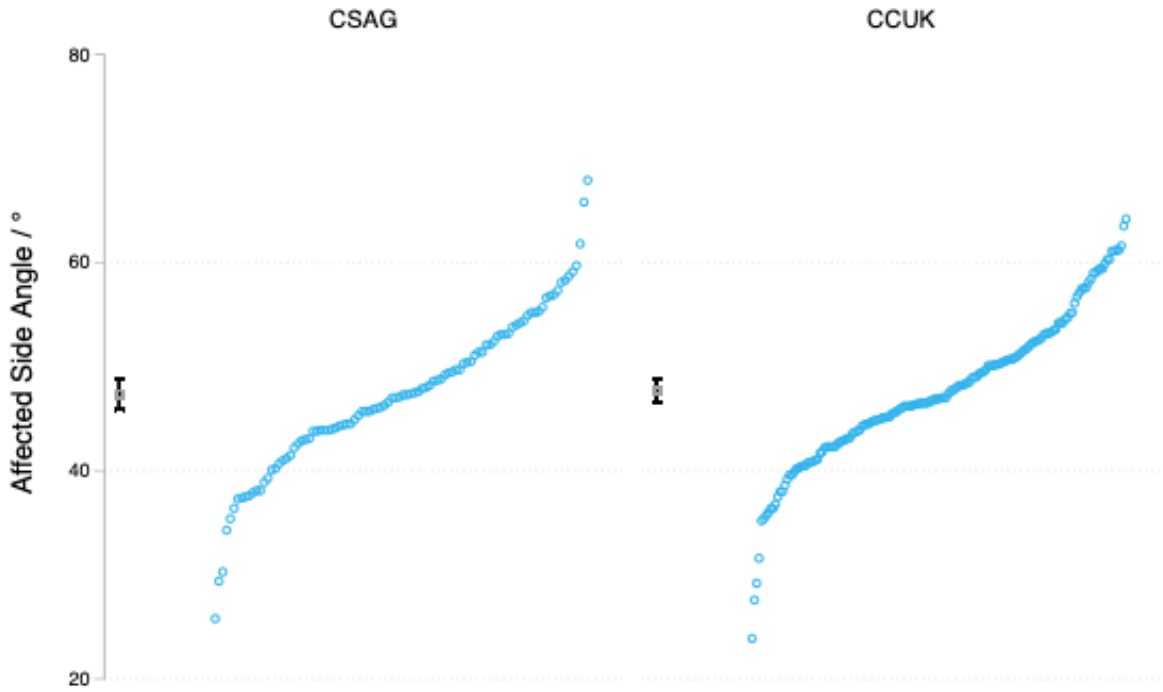

Figure 25. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts affected side angle measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	100	47.35	7.52	45.86 to 48.84	0.749
CCUK	161	47.65	7.26	46.52 to 48.78	

Table 16. Table to display the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the affected side angle, along with the estimated p value.

The data from both cohorts show a similar distribution. The mean value was smaller in the CSAG cohort, although the difference between the means was 0.3 degrees. There was no statistically significant difference between the two cohorts.

Non-affected Side Angle Measurement

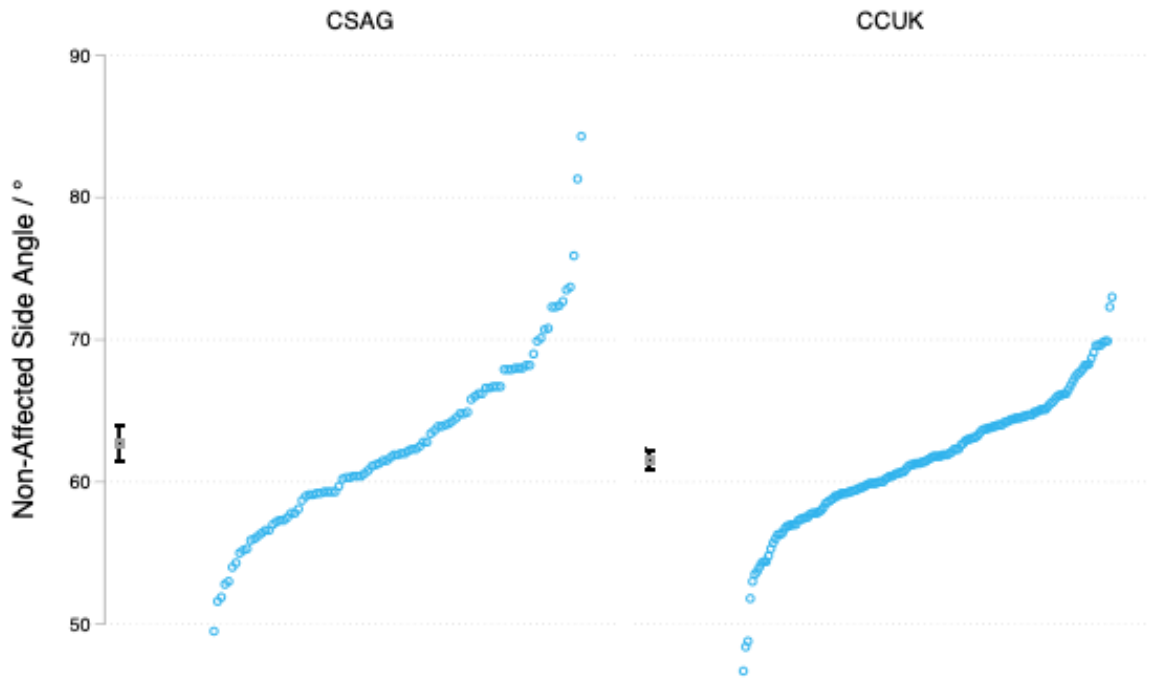

Figure 26. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the mean for the CSAG and CCUK cohorts non-affected side angle measurements.

Cohort	No. of models	Mean/mm	SD	95% Confidence Interval	p value
CSAG	101	62.70	6.19	61.48 to 63.92	0.082
CCUK	162	61.54	4.52	60.84 to 62.25	

Table 17. Table to display the cohort numbers, mean, standard deviation and 95% confidence intervals of the mean for the CSAG and CCUK cohorts for the non-affected side angle, along with the estimated p value.

The data for non-affected side angle measurement for both cohorts shows a similar distribution. The observed mean was smaller in the CCUK cohort by 1.16 degrees compared with CSAG. This difference was not a statistically significant.

Table 18 provides a summary of the comparisons between the CSAG and CCUK five year old maxillary arch models for all of the linear and angular measurements along with their statistical and clinical significance.

Measurement	**Greater Mean**	**Difference in means /mm or degrees**	**Statistically Significant (p value)**	**Clinically significant**
Anterior Width	CCUK	0.76	Y (0.044)	N
Anterior Depth	CCUK	0.42	Y (0.029)	N
Affected side C	CCUK	1.04	Y (0.004)	Y
Non-affected side C	CSAG	0.24	N (0.184)	N
Posterior Width	CCUK	1.23	Y (0.003)	Y
Posterior Depth	CCUK	0.55	N (0.073)	N
Affected side E	CCUK	1.03	Y (0.002)	Y
Non-affected side E	CCUK	0.14	N (0.599)	N
Arch length	CSAG	0.19	N (0.485)	N
Affected side angle	CCUK	0.3	N (0.749)	N
Non-affected side angle	CSAG	0.16	N (0.082)	N

Table 18. Summary of comparison of cohort findings along with the statistical and likely clinical significance.

4.4 Analysis of Sides

When analysing the cleft affected and cleft non-affected sides, these can be considered irrespective of which cohort they belong to.

4.4.1 Analysis of sides respective of cohort

In order to analyse the data it was restructured into a form suitable for a linear mixed model analysis. This is of use where there is variation among and between groups and allows analysis of the differences between the means of each group.

Figures 27 to 29 are margin plots which illustrate the interaction between the cohort with the affected and non-affected side. The graphs also give the 95% confidence intervals of the mean for each side.

Affected C and non-affected C measurements

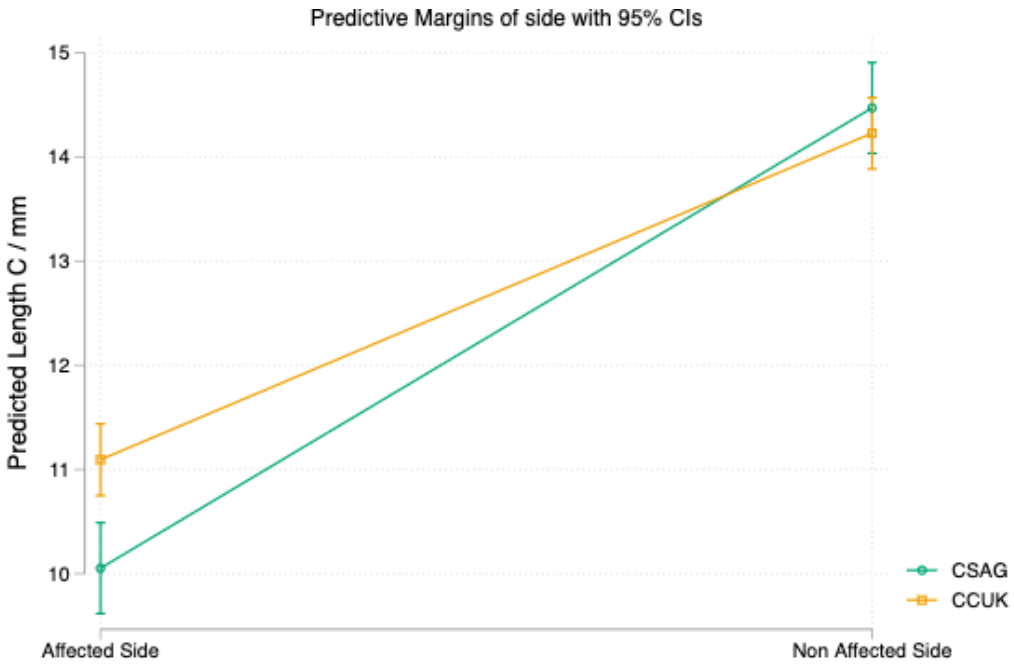

Figure 27. Margin Plot illustrating the interaction between the CSAG and CCUK cohorts on the affected side C measurement and non-affected side C measurement.

The margin plot (Figure 27) shows that both cohorts have lower values for the C measurement in the case of the affected side than the non-affected side, with the affected side measurement being smaller in the CSAG cohort. This difference is significant as the 95% confidence intervals of the means do not overlap. When looking at the non-affected side, the values are greater than with the affected side in both cohorts. However, the difference between the CSAG and CCUK cohorts is less and, in this case, the 95% confidence intervals overlap. The plot also indicates there is a significant interaction of side and cohort (p=0.001).

Affected E and non-affected E measurements

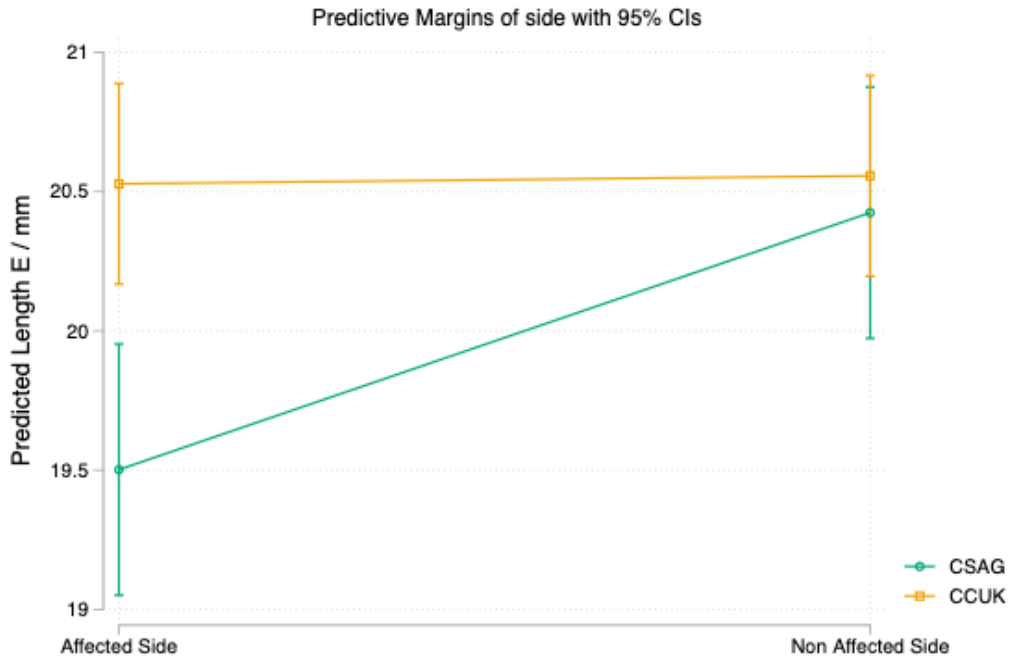

Figure 28. Margin Plot illustrating the interaction between the CSAG and CCUK cohorts on the affected side E measurement and non-affected side E measurement.

The margin plot (Figure 28) shows that the CSAG cohort has a lower value for the E measurement on the affected side compared to the CCUK cohort, with no overlap of the 95% confidence intervals. For the non-affected side, the values are greater, but the difference between the two cohorts, CSAG and CCUK, is much smaller and with overlap of the 95% confidence intervals. For the CCUK cohort there is no difference between the affected E and non-affected E values, unlike the CSAG cohort. The interaction of side and cohort is statistically significant different (p=0.032).

Affected side and non-affected side angle measurements

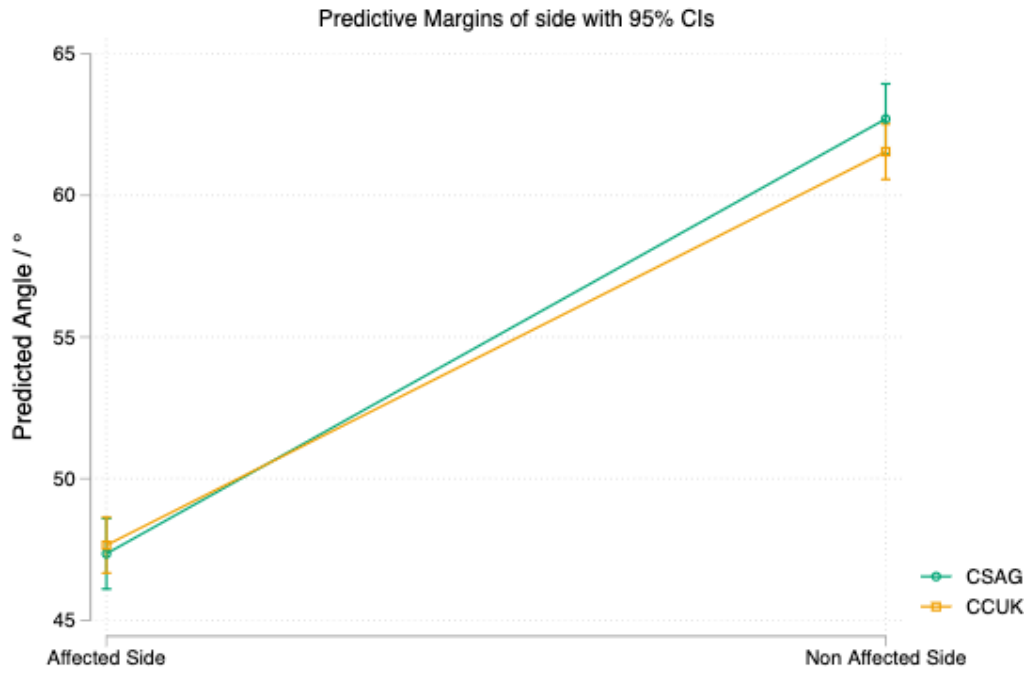

Figure 29. Margin Plot illustrating the interaction between the CSAG and CCUK cohorts on the affected side angle measurement and non-affected side angle measurement.

The margin plot (Figure 29) shows that both study cohorts have lower values for the affected side than the non-affected side and with the 95% confidence intervals overlapping

in both cases. The interaction of side and cohort is not statistically significant different (p=0.202).

4.4.2 Analysis of sides irrespective of cohort

The following plots, Figures 30 to 32, allow visualisation of the means, associated 95% confidence intervals of the means, and the cumulative data distribution for the combined cohorts (CSAG and CCUK) for each of the three measurements (C, E and Angle) respectively. The calculated p value is a probability from the two-sample t-test comparing the two sample means for each measurement (C, E and Angle).

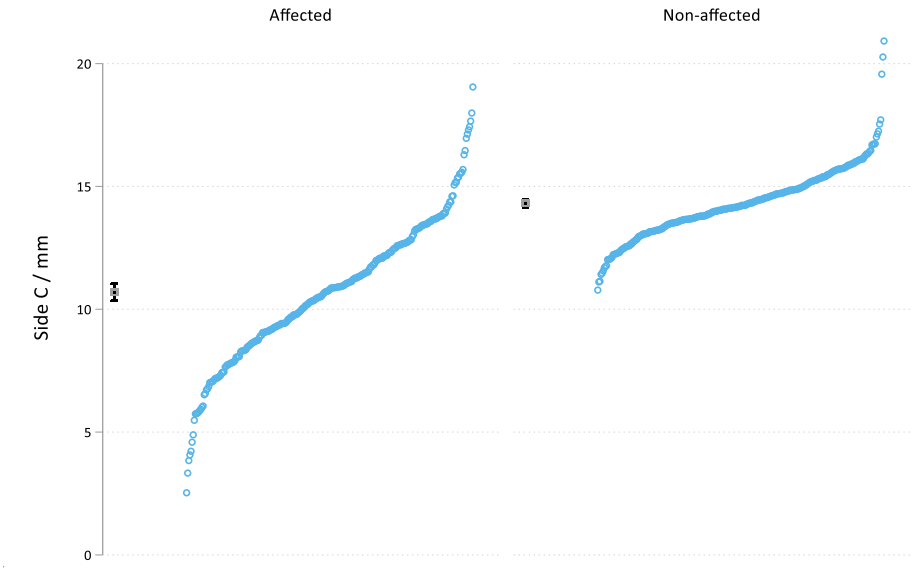

Figure 30. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the means of the affected versus the non-affected side of all the models at the level of the C.

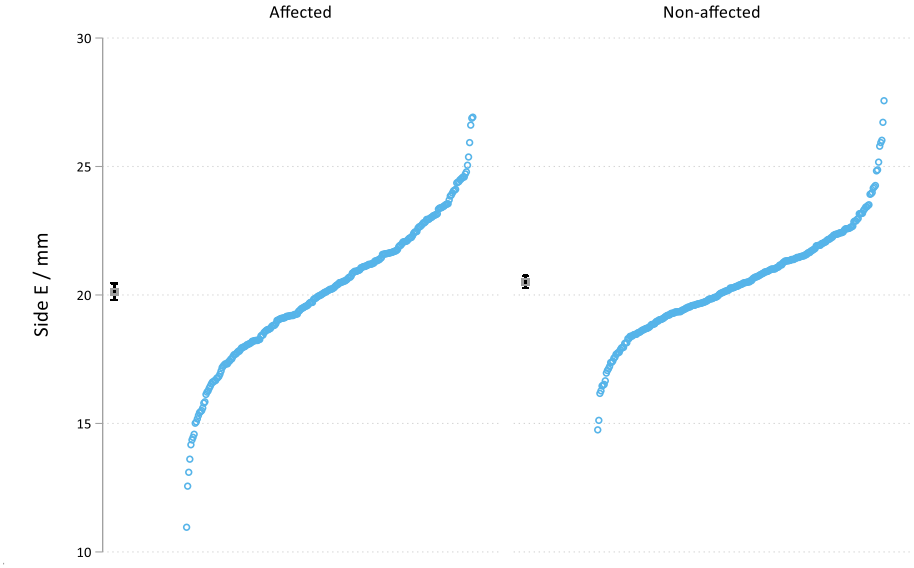

Figure 31. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the means of the affected versus the non-affected side of all the models at the level of the E.

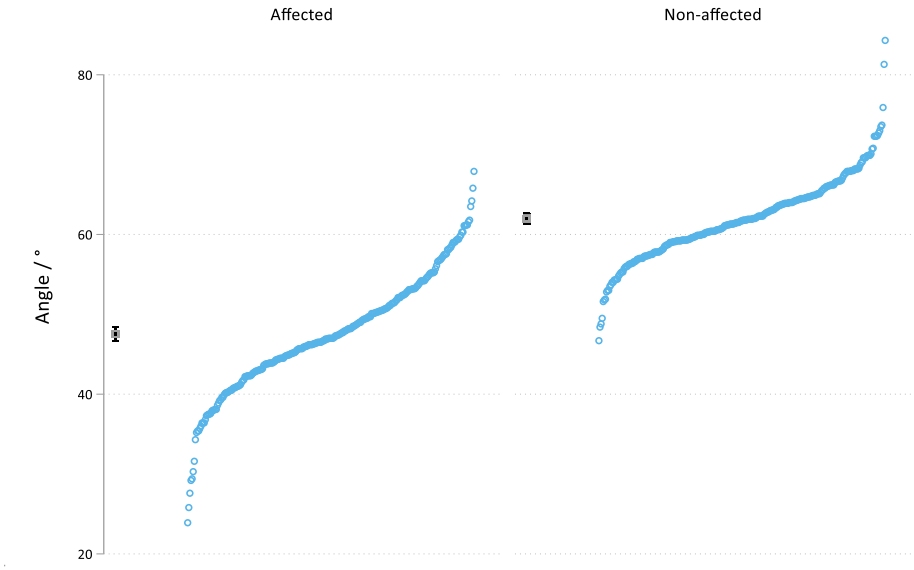

Figure 32. Graph showing the raw data, distribution, mean and associated 95% confidence intervals of the means of the affected versus the unaffected angle of all the models.

Measurement	Number Observed	Mean /mm or degrees	Standard Deviation	95% Confidence Interval	p value
Affected side C	261	10.69	2.85	10.35 to 11.04	<0.001
Non-affected side C	262	14.32	1.43	14.15 to 14.5	
Affected side E	267	20.13	2.7	19.80 to 20.45	0.068
Non-affected side E	267	20.51	2	20.26 to 20.75	
Affected side angle	261	47.54	7.35	46.64 to 48.43	<0.001
Non-affected side angle	263	61.99	5.24	61.35 to 62.62	

Table 19. Table showing the linear and angular measurements of canine and second deciduous molar to sagittal plane for the affected and non-affected sides for the combined cohorts.

The plots (Figures 30 to 32) and data summary in Table 19 show comparison of sides irrespective of cohort. For the C measurement (Figure 30) and the angle (Figure 32), the plots show less similar distribution of the data in each case, with there being a statistically significant difference between the affected and non-affected sides in the case of both the C measurement and the angle ($p<0.001$).

The data for affected versus non-affected side E measurement shows a similar distribution (Figure 31) but there was no statistically significant difference between the two ($p=0.068$).

5 DISCUSSION

5.1 Overview

This study comprised an investigation into the transverse dimensional changes between two cohorts of children born with a unilateral cleft lip and palate and who were treated in the UK between the mid 90's and early 2010's. It was completed by using direct digital measurement of the maxillary models of the cleft affected children taken at the age of five years. A total of 292 models were digitally laser scanned and interrogated. Agreement analysis was undertaken and comparative results between both the cohorts and cleft affected and non-affected sides determined.

5.2 Development of the Method

The evaluation of some of the changes to patient outcomes between the CSAG and CCUK cohorts has previously been documented within the results of the CCUK study (Ness *et al.* 2015). These include changes in dental relationships with facial growth, speech, parental report of self-confidence, dental health and hearing. The antero-posterior dental relationships were studied using the articulated upper and lower study models with 5-Year Olds' Index (Atack *et al.* 1997). In the current study, in order to assess changes and therefore potential differences in the maxillary transverse dimensions between the two cohorts, the maxillary models were considered in isolation rather in combination with the mandibular models.

From the literature review it was evident that various methods of assessing arch width, length and shape have been utilised by researchers, employing both analogue and digital techniques. The decision was taken to conduct this study in a digital workspace, which has

been shown to be both accurate and reliable (Fleming *et al.* 2011, Lemos *et al.* 2015). The use of OrthoAnalyzer™ software was chosen due to ease of access and compatibility with the 3 Shape R700™ Orthodontic Scanner used to create the digital images.

All of the studies identified in the literature review had used linear measurements (Bishara *et al.* 1997, Wojtaszek-Slominska *et al.* 2010, Generali *et al.* 2017, Smahel *et al.* 2004, Ruskova *et al.* 2014, Mishima *et al.* 1996), some used angles (Wojtaszek-Slominska *et al.* 2010, Mishima *et al.* 1996) and others used volumes (Generali *et al.* 2017) in the assessment of the maxillary arch. The OrthoAnalyzer™ software used in this study not only allowed for linear measurements and the construction of angles, but also the construction of theoretical planes (i.e. sagittal plane), facilitating model orientation and measurements to and from these planes. In measuring the angles, small errors were likely due to the difference in vertical height of the cusp tips of the teeth in the various models, which were used as the reference points for construction of lines of measurement in each case (i.e. these angles are not constructed on the occlusal plane but on the 3 points of the model). However, it was felt this would be small and consistent in the case of all the models and would not affect the interpretation of the results to any significant extent.

The determination of volumes using reverse engineering was also considered as a potentially useful measurement of treatment outcome as has recently been reported by Generali *et al.* (2017) and Monga *et al.* (2020). The latter compared unilateral (UCLP) and bilateral cleft lip and palate (BCLP) subjects and found that the palatal volumes of UCLP and BCLP were significantly smaller than that of the control group. The mean age of the control group was 12.9 years compared to 10.33 and 10.44 for the UCLP and BCLP respectively. This difference in age could be an additional reason for the differences in the data. Furthermore,

boundary identification to enclose a volume where the arch is incomplete is subjective. This, along with the models in this study not always being a true representation of the palatal form (described in influence of model artefacts) meant it was decided such measurements were not only likely to be inaccurate, but the findings would not necessarily be useful and could indeed be open to misinterpretation. For example, a wide shallow palate might contain the same volume as a deep narrow palate and the single measure would not be able to differentiate between the two, especially as the differences in our cohort were potentially more subtle than that of Monga *et al.* (2020) or Generali *et al.* (2017).

5.3 Agreement

In order to ensure the repeatability of the results, agreement measurements were undertaken on 30 randomly assigned models. These values were tested using both Lin's concordance correlation coefficient and interclass correlation coefficient (3,1). Lin's concordance correlation coefficient combines measures of both precision and accuracy by considering how far the observed data are from the line of perfect concordance. The closer the line of best-fit to the line of perfect concordance the more accurate the data, and the lower the data scatter about the best fit line the higher the precision. Lin's coefficient increases with increasing accuracy and precision to a limiting value of 1 for perfect concordance. For all but one measurement, the Lin's values were greater than 0.9 and for all but two, greater than 0.95. This indicates high accuracy of the data. The measurement where the accuracy was the worst (0.808) was the non-affected side C. It was often seen on the models that the canine teeth were significantly worn, which may explain the difficulty in accurate repeatability of this measurement. Figures 14 and 15 show the scatter of the data points around the line of best fit and the outliers are clearly identified. It is of note the

outliers that were highlighted in non-affected side C and non-affected side E data were both from the same model (475). On review of this model there was significant wear of all teeth, increasing the challenge of valid landmark identification.

An Intraclass Correlation Coefficient (3,1) was also conducted on the data. This specific ICC (3,1) was appropriate for this study as each model was randomly selected from all possible models, and was measured by the same set of observers, with these observers being the only ones of interest. The values from this test were in-keeping with the results of the Lin's concordance correlation coefficient, and showed that those with the lowest Lin's concordance correlation coefficient values and ICC (3,1) had the largest 95% confidence intervals, indicating greater imprecision.

5.4 Interpretation of the results

5.4.1 Comparison of cohorts

Of the 11 linear and angular measurements, five showed statistically significant differences between the cohorts where the CSAG measurement was smaller than the CCUK measure. Those which showed a statistically significant difference, with a difference in the mean of less than 1mm, were the anterior width (p=0.044) and anterior depth (p=0.029). Those which showed the greatest statistically significant difference were the affected side C, posterior width and affected side E (p= 0.004; p=0.003; p=0.002). In all cases the difference in the means was greater than 1mm, indicating clinical significance. The overall findings are summarised in Table 18. Where the means showed the CSAG values to be greater than those of CCUK, the differences were not statistically or clinically significant.

5.4.1.1 Anterior Segment

Both the anterior width, depth and affected side C measurements showed statistically significant differences, with the CCUK cohort having greater mean values than the corresponding CSAG measures. The anterior dental segment is greatly affected by the cleft and so an increase in the CCUK values might suggest an improvement in archform. Previously reported values for intercanine width of a non-cleft population at the age of five years are 28.4mm for girls and 30.3mm for boys (Bishara *et al.* 1997). In the sample from this study, the mean intercanine widths were 24.7mm for CSAG and 25.5mm for CCUK. Although both are still below the average for the non-cleft child, the mean intercanine width for the CCUK cohort was closer to the norm for the unaffected child. The proximity of the affected side C to the midline is the likely cause of the mean intercanine width being reduced in the cleft affected child. This is illustrated by the means and 95% confidence interval of the means for the cleft affected (10.6mm, 1mm) and unaffected sides (14.4mm, 0.5mm) respectively when the CSAG and CCUK groups are combined. It can also be shown that if the unaffected side measurement is doubled (28.8mm) this value sits between the male and female average values for a non-cleft population. This difference is also clearly seen in Figure 30, where the affected and non-affected sides are considered irrespective of the cohort to which they belong. The reduction in the affected side C value is due to the collapse towards the midline of the lesser segment, most likely as a result of the surgical scarring at the cleft repair site. Therefore, the CCUK value being clinically and statistically greater than the CSAG indicates improvement in the anterior segment outcome for the CCUK cohort.

The comparison of affected and non-affected side C measurements was also considered with respect to their cohorts using a margin plot (Figure 27). This plot illustrates that the on

the affected side the means and 95% confidence intervals do not overlap whereas on the non-affected side they do. This would further confirm that it is the cleft and its repair that is the significant event and that this has a lesser effect in the CCUK cohort. Therefore, showing there is an overall improvement in outcomes for the CCUK cohort again.

The anterior depth measurement is reported as statistically significantly different (p=0.029), where CCUK is greater than CSAG and the difference in the mean is 0.42mm. This is in line with previous published work (Wojtaszek-Slominska *et al.* 2010). However, there were some issues with recording this measurement, which is discussed further in the influence of model artefacts section, and so the results should be interpreted with some caution.

5.4.1.2 Posterior segment

Within the posterior segment the posterior width and affected side E measurements both showed the CSAG and CCUK cohorts to be statistically significantly different, with the CCUK mean values being greater. The respective difference in mean values of 1.23mm and 1.03mm were also clinically significant. The posterior depth and non-affected side E measurements were not significantly different. The latter finding is in-keeping with a previous study by Generali *et al.* 2017, although they found no statistically significant difference in the posterior width between a cleft and non-cleft cohort. This finding may not be directly transferable to the current study as their cohort was slightly older at 9 years of age. Prior to this, and similar to the current study, Mazaheri *et al.* (1971) found at 5 years of age the upper posterior arch width and inter-canine width was reduced in a CLP group compared to non-cleft participants. Also, most of the cleft affected children demonstrated a decreased maxillary width, which was more evident than the decrease in maxillary arch

length. It might be the case then that this reduced posterior arch width is not maintained with continued facial growth.

Comparing the UCLP populations in this study to non-cleft population values for posterior arch width, Bishara *et al.* 1997 provides values of 40.8mm for girls and 43.5mm for boys. The CSAG mean in the current was 40mm, which is just below the female value, whereas the CCUK mean was 41.2mm. This would indicate that posterior arch width is normalising from the CSAG to the CCUK cohort.

Similarly, to the anterior segment finding, the difference in posterior arch width appears to originate from the reduction of the affected side E measurement to the midline for the CSAG cohort. Whilst the CSAG non-affected side E 95% confidence interval ranges from 20mm to 20.9mm, the affected side has a range of 19mm to 20mm. Whereas for the CCUK cohort their ranges overlap with non-affected being 20.3mm to 20.8mm and 20.1 to 20.9mm for affected. This is demonstrated clearly in Figure 28 where the CCUK cohort shows that the affected and non-affected side measurements are very similar. Therefore, indicating the improvement seen in surgical repair of the CCUK ULCP children as compared to the CSAG cohort.

Overall the findings would suggest that the effect of the cleft and its repair has anterior and posterior implications for transverse arch dimensions, with the greater impact being seen in the CSAG group, whereas improvements towards equalisation and normalisation are seen in the CCUK group.

5.4.1.3 Arch Length

Whilst the CSAG mean value for arch length was slightly higher (0.19mm) than the CCUK value, this was not statistically or clinically significant. Past studies have also shown that

arch length is less affected by the presence of a UCLP (Mazaheri *et al.* 1971). Wojtaszek-Slominska *et al.* (2010) considered the effect of early gingivopalatoplasty on the developing arch form compared to those of a cleft population who did not undergo gingivoplatoplasty. They found that arch length significantly decreased with this procedure and gave an average value of 27.09mm for the control group. In the current study the mean values were lower at 25.1mm for CSAG and 24.9mm for CCUK, which may be a result of the landmarks used to measure the arch length, which were different in the current study.

5.4.1.4 Angle

When considering the angles for both the affected and non-affected sides, no statistical difference was seen between the CSAG and CCUK cohorts. This was to be expected for the non-affected side and reflects the lack of statistical difference in the other non-affected side measurements. However, for the affected side this was not expected, but might be explained by considering Figure 33. The line AB is drawn perpendicularly from the midline to the mesiobuccal cusp of the 2nd primary molar (affected side E); a similar perpendicular line, CD, is drawn from the midline to the canine (affected side C); x and y are the lengths of AB and CD respectively; and, line DB subtends angle Ω from point A. The size of angle Ω is related to the difference between x and y (the cosine of Ω is proportional to this difference). It therefore follows that if the primary molar and the canine are both moved towards the midline by the same amount then the difference between x and y will be unchanged and the angle Ω will remain the same.

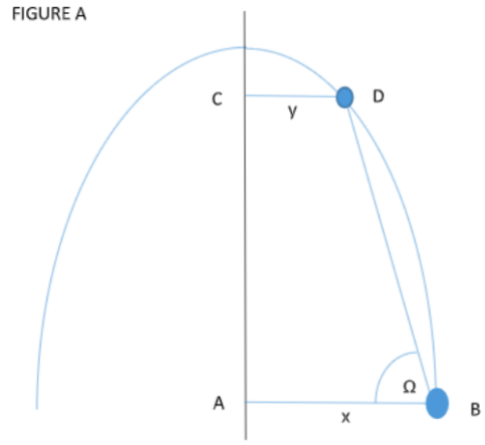

Figure 33. Diagram showing how the angle is affected by the distance to the midline of the canine and molar.

As the difference between the means of the CSAG and CCUK affected side C was 1.04mm and affected side E was 1.03mm the distances x and y in Figure 33 have changed by almost the same amount and so the angle will remain the same.

When considering the affected and non-affected side irrespective of cohort, Figure 32 illustrates the distribution of the raw data and confirms a statistically significant effect ($p < 0.001$), indicating the significant difference between the larger non-affected side angle and smaller affected side angle. This again indicates that the lesser affected cleft segment is collapsed towards the midline following surgical repair.

5.5 Reasons for improvement

A clinical and statistically significant difference between the CSAG and CCUK cohorts is seen with three of the transverse measurements (affected side C, affected side E and posterior width) considered in this study, showing that there has been improvement in the maxillary transverse dimension. Changes to surgical protocol, experience and technique may be the

reason for this. It has previously been reported that improved surgical outcomes in cleft affected children are associated with the surgeons performing a higher number of surgical repairs (Al-Ghatam *et al.* 2015). A study which assessed team composition by Scott *et al.* (2015) found that of the 18 primary cleft surgeons, 16 were reaching the target of 40 cases annually. The two who did not, nevertheless operated on 35 each. This is hugely different from the CSAG findings where only 17 of the 83 surgeons operated on more than five babies over a two-year period.

A further difference to the way these UCLP babies were treated is with the adoption of the Oslo Surgical protocol for repair. This has been shown to have improved outcomes for craniofacial morphology and nasio-labial appearance (Fudalej *et al.* 2015, Brattström *et al.* 2005). It involves a Millard lip repair and anterior hard palate repair with a single layer Vomer flap at three months of age, followed by hard and soft palate repair at nine months, using a modified von Langenbeck technique. The timing of this technique aims to provide a balance between allowing favourable facial growth with adequate speech development.

Finally, surgical training is now via a structured pathway in the UK, either through oral and maxillofacial surgery or plastic surgery craniofacial fellowships. This training is vital in gaining experience as Rautio *et al.* (2017) found in a study, which compared timing of different surgical techniques. They reported that whilst statistical evidence did not prove that any technique was better, they did say that the surgery itself was more problematic for surgeons who were still gaining experience with an unfamiliar surgical protocol. Therefore, indicating the need for structured training programs aimed at gaining experience and learning from mentors.

5.6 Study Critique

This study, to determine whether the transverse dimensions of maxillary unilateral cleft lip and palate affected children has improved since the implementation of the CSAG recommendations, was undertaken as a retrospective cohort study using information which was already in existence prior to commencement of the study. The retrospective nature of this method has advantages and disadvantages, which will now be discussed.

5.6.1 Sample selection bias

An element of sample selection bias was present in this study as not all of the original CSAG models were available to be included. It is understood that the models may have been previously loaned to other researchers and were either not duplicated, or not returned as a complete set. Without knowing what this other research concerned, and whether cases with specific features were selected and not returned could mean there is some selection bias in our study. However, the high number of models included and the variation in morphology means that it is unlikely selection bias has affected our results.

With the CCUK cohort all of the models that had been obtained were available to be included in the study. However, of the 216 patients born with UCLP in 2008 (CRANE 2013), records were only taken for 176. This could be due to not wishing to be included in CCUK data collection or it might reflect the difficulty in obtaining impressions of five-year olds. CRANE reported in 2009 that their rate of non-consent from parents was 3.8% (CRANE 2010). Again, the overall number that were finally included in the current study from the CCUK cohort was representative of the whole cohort.

5.6.2 Measurement bias

All of the measurements, including the repeatability measurements were undertaken by a single researcher (CM). This researcher (CM) also completed all the scanning of the models. At the scanning stage previous markings on the models meant it was obvious which models belonged to which cohort and were labelled as such. However, all the scanned models were subsequently anonymised and given a unique identifier code by a laboratory technician, which meant the researcher was blind to the cohort allocation when conducting the measurements on screen.

5.6.3 Influence of model artefacts

On a number of the models it was evident that the true anatomical morphology of the patient was not represented by their model. Examples of this include: the imprint of gauze in the palate, the imprint of gauze of the alveolar ridge and an abnormally smooth palatal surface. This may infer that an oronasal fistula was present at the time the impression was taken and so gauze was placed to protect the nasal cavity during impression taking, or the resultant impression was smoothed by the operator following removal of the impression from the oral cavity. This has three implications in this study. Firstly, if the gauze was covering teeth to be used for measurements this model was excluded as the landmarks were not visible. Secondly, where gauze was present in the palate this would give a false measurement for the anterior and posterior depths. In retrospect, these models should have been excluded for the same reason as above. Lastly, if repair of the palate had been unsuccessful and incomplete then this may have an effect on the growth of the maxilla, as it is likely that less scarring was present and so the surgical repair may be less evident.

There were also a number of cases where the researcher (CM) noted from the model that it appeared as though the cleft had not been completely repaired. This was the case in model numbers 15 of CCUK (8.5%) and 7 of CSAG (6%).

5.6.4 Influence of missing data

A number of the models had missing teeth, or meaningfully worn teeth that would not allow direct measurements or construction of planes. As each measurement was treated separately, it meant that on some models (four from each cohort) no measurements at all were possible and others may have incomplete data sets as set out in Table 6. However, the number of models where this effect was evident was approximately the same in each cohort, but slightly greater proportionally in the case of CSAG. The most likely cause of missing teeth for this population would be early childhood caries. This reasoning is supported by the CCUK study, which showed no improvement in the children being caries free when compared to the CSAG study (Smallridge *et al.* 2015).

5.7 Implications and suggestions for further research

In conducting this study, a digital record of the CSAG and CCUK maxillary models and the valuable information they hold has been created for further audit and research.

This study has shown that for three of the transverse dimensions measured on the maxillary models, the outcomes for the CCUK cohort are clinically and statistically significantly improved compared to the earlier CSAG cohort. This implies that recommendations following the CSAG investigation have had a positive influence on the surgical repair. This is through more formalised surgical training, increased surgeon workload and therefore

experience and finally a more consistently applied surgical protocol. As with recent studies comparing outcomes from the time of CSAG to the time of CCUK, this positive information should be fed back to the cleft teams both in the UK and Worldwide.

This study has also shown that certain measurements were not of great value, being at the mercy of model artefacts. In particular, anterior and posterior depths as well as arch length. Since model collection or intra oral scanning of five-year old UCLP patients will continue as part of the protocol of routine cleft care, the addition of a transverse maxillary assessment to the already used 5-Year Olds' Index will add to the ongoing body of evidence for future studies on outcome. Further research could establish an efficient, reliable method of obtaining the required data from the digital models.

6 CONCLUSIONS

6.1 Conclusions

The null hypothesis was rejected as there was a statistically significant difference between the CSAG and CCUK cohorts for five of the eleven measurements.

The quantitative differences were deemed to be clinically significant for the affected side C, posterior width and affected side E measurements.

Where non–cleft norms were available, both the CSAG and CCUK cohorts were reduced for the anterior width, whereas the CCUK cohort was approaching normalisation for the posterior width.

Overall the study has found improvements for the measured outcomes for children born with UCLP in more recent years. Clear differences remain between the cleft affected and not affected sides of the maxilla.

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8 APPENDICIES

APPENDIX 1: University of Bristol Study Registration

University of BRISTOL

University Hospitals Bristol NHS
NHS Foundation Trust

Cleft, the transverse dimension: CSAG vs CCUK

Principle Applicant: Charlotte Molyneaux

Scientific outline

Aim: To determine changes in the transverse dimensions of maxillary unilateral cleft lip and palate patient populations between the CSAG and CCUK studies.

Design: Retrospective analysis of data collected by the CSAG and CCUK projects.

Population: All available models from five-year-olds with nonsyndromic UCLP from CSAG and CCUK projects.

Ethics: The original CCUK study obtained full ethical approval (REC reference number 10/H0107/33, South West 5 REC).3

The project has been registered as service evaluation with UH Bristol.

Data collection and management: CSAG and CCUK maxillary models will be digitally scanned. Measurements of the intercanine, intermolar and palatal depths will be gained. The arch shape of the maxillary models will also be described.

As both the studies collected data from unilateral cleft lip and palate patient populations at the age of 5 years this will allow assessment of the transverse dimension prior to any significant orthodontic intervention. Thus, the findings will give an impression of the surgical success of the cleft repair.

Study Limitations: Accuracy of data collection by CSAG and CCUK. Accuracy of digital plotting of identified points. Sample size.

Research Management: The investigator will perform this study based at the Royal United Hospital Bath and the Bristol Dental Hospital under the direction and supervision of Professors Sandy and Ireland and Dr Waylen. Results of this research will be written up as a DDS project as well as scientific papers submitted for publication in peer-reviewed journals.

Keywords: Complete unilateral cleft lip and palate, CSAG, CCUK, transverse dimension, maxilla.

APPENDIX 2: Clinical audit proposal form for service evaluation.

University Hospitals Bristol NHS
NHS Foundation Trust

ID No: SE 180
(office use only)

CLINICAL AUDIT PROJECT PLAN

All clinical audit projects should be registered before they start.

- Please discuss your proposal with the appropriate Clinical Audit Facilitator.
- Contact details and guidance on completing this form are available via relevant workspace
http://connect/governanceandquality/clinicalauditandeffectiveness/clinicalaudit/Pages/Carrying%20out%20projects.aspx

Title (see note 1)					
A service evaluation of the transverse dimensional changes in unilateral cleft lip palate patients from two cohorts.					
Your Details: Audit lead					
Name	Charlotte Molyneaux	**Division**	Surgery, Head & Neck		
Position/Job Title	Orthodontic Registrar	**Specialty**	Orthodontics		
Email	charlotte.molyneaux@bristol.ac.uk	**Tel**		**Bleep**	

Project Team (see note 2)

Name	Job Title	Specialty	Role within Project (data collection, Supervisor etc)
Professor Sandy	Dean – Health Sciences	Orthodontics	Supervisor
Professor Ireland	Honorary Consultant	Orthodontics	Supervisor
Dr Waylen	Senior Lecturer in Social Sciences	Social Sciences	Supervisor

Participation details (see note 2)

What areas will this audit impact on? (e.g. another profession/specialty/Trust)	Who in this area have you discussed and agreed this audit with?		
	Name	Job Title	Date Agreed
Cleft services	Vanessa Marshall	Manager NIHR – CCUK study team	27.09.18

Background (see note 3)

The CSAG national audit was carried out more than 20 years ago and was designed to determine whether cleft outcomes in the UK were poorer than those in other developed nations. The CCUK audit was carried out in 2012, some 15 years later in order to determine whether outcomes had improved given the changes to the cleft service. Since the recommendations put forward by CSAG 1998 have been adopted by the cleft community the training, caseload and team composition has changed. The improvement in certain outcomes has been documented by the CCUK study. However, the dentoalveolar relationships have only been assessed by the somewhat subjective 5-year-olds index. Using the study casts collected from these two nationwide projects the transverse dimensional changes will be digitally assessed. The effects of primary surgery can have a huge impact on function, aesthetics and dentoalveolar development, thus this project will give an indication as to whether the restructuring of cleft services, and specifically surgery, has resulted in improved outcomes.

Aim (see note 4)

The aim of this project is to determine what, if any changes have occurred in the transverse dimensions of maxillary unilateral cleft lip and palate patient populations between the CSAG (1998) and CCUK (2012) audits?

Objectives (see note 4). You may find it is unnecessary to use the "Objectives" section i.e. "Aim" and "Standards/Criteria" may cover all the essential information.

1. Deduce the quantitative differences in the intermolar width, and intercanine width between the two populations.

2. Deduce the quantitative differences in the anterior palatal depth, mid palatal depth and posterior palatal depth between the two populations.

3. Describe the arch shapes identified using mathematical data and thus deduce the differences in arch shape between the two populations.

4. Where possible compare these to existing data of children of a normal population.

Standards/Criteria

Please list standards as per example in first row.

- Provide full information on source of standards – Title, website reference etc.
- Be sure data you plan to collect will measure performance against listed standards.

	Criteria	Target (%)	Exceptions	Source & Strength* of Evidence		Instructions for where to find data
1	**SERVICE EVALUATION – not measuring against clinical audit standards at this stage**					
2						
3						
4						
5						
6						

***Strength of Evidence**

A At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation

B Availability of well-conducted clinical studies but no randomised clinical trials on the topic of the recommendation

C Expert committee reports or opinions and/or clinical experience of respected authorities. Absence of directly applicable clinical studies of good quality

D Recommended good practice based on clinical experience (local consensus)

Data Collection Methodology (see note 5)			
Casenote review ☐	Prospective data collection ☐	Data from existing database(s) ☒	Patient/ staff questionnaire ☐

Further details or other method	Use of maxillary models from the CSAG and CCUK studies
Please give details of how this has been/will be piloted:	Initial measurements of 5 models from the two data sets will be undertaken. Issues identified will result in adjustments to the method.

- **Please include your data collection form/spreadsheet with this proposed Audit Plan.**
- **Be sure the data items you're collecting match the standards set**

Audit Sample (see note 6)	
Sample selection criteria *(i.e. type of patients*	Unilateral cleft lip palate patients from CSAG and CCUK studies within the 5 year old age group.
Time period to be audited *(i.e. Jul14 - Oct14)*	October 2018 – October 2019
Estimated number of cases *(as a guide 30 -50 should be sufficient)*	100 + for each cohort
Who will provide list of patient (NB – need appropriate hospital / NHS numbers)	Not required – anonymised models available from cleft services
If you are requesting notes through the CA team, where would you like them delivered	Not required

Timescale/Deadlines (see note 6)	
Proposed start of data collection	October 2018
Proposed date for presentation of results	July 2020
Forum	DDS write up.
Proposed finish date *i.e. after report and action plan produced*	September 2020

Will you be leaving your current post in the near future?	No
If Yes, please give leaving date	
If your project will not be finished by then, please identify and provide the name and job title of another member of staff who is willing to take over when you go	
Are there any other deadlines you need to take into consideration?	
Is there any intention to publish your results (If yes, please give details)?	**Yes – peer review journal.**

You will need an appropriate senior clinician / manager to support the project.
Please indicate over the page the date that this has been agreed.

Project Lead

- I agree to ensure that this project is completed, the results disseminated, and a report given to my Clinical Audit Facilitator.
- I confirm that the standards outlined within this proposal are suitable to measure the quality of care provided for this group of patients
- I understand that non-anonymised (staff/patient) audit data must not be taken outside the Trust and will act in accordance with the Data Protection Act / Caldicott Principles at all times.
- I understand that audit results belong to the Trust and that a project report may be made available to anyone who requests it.

Charlotte Molyneaux	10/10/2018
Project Lead	Date

Senior Clinician / Manager

- I confirm that this project has been agreed as part of the Specialty audit programme and that I will give my full support to it.
- I will ensure the dissemination of audit results and lead on the development and implementation of an action plan (if necessary) in order to obtain improvements in the quality of care provided.

Professor Anthony Ireland	24/10/2018
Senior Clinician / Manager	Date

Clinical Audit Convenor

- I approve the project described above and confirm that it has been appropriately reviewed for methodological quality, resource implication and importance to the Trust.

[redacted]	24/10/2018
Clinical Audit Convenor	Date

Once you have completed this form, please email it to the relevant Clinical Audit Facilitator, copying in your Senior Clinician / Manager

- If this project is approved, the information on this form will be entered onto the Clinical Audit Project Management database.
- You will be asked to complete a final report and action plan once the results of your audit are known. Detail of these will also be entered on the database.

APPENDIX 3: CCUK Resource Research Proposal Form

CCUK Resource Research Proposal Form

Collaborator's outline project proposal (using existing CCUK data or collection of new data).

1. Applicants

Principal applicant	Name:	Charlotte Molyneaux
	Affiliation:	University of Bristol
	Email:	charlotte.molyneaux@bristol.ac.uk
	Telephone:	
	Address:	DDS Room, CDH, Bristol Dental Hospital, BS12LY
Co-applicants	Names:	Professor Ireland, Professor Sandy, Dr Waylen

2. Project

Project title (no more than 120 characters with spaces):	Cleft, the transverse dimension: CSAG vs CCUK
Start date:	October 2018
End date:	October 2019

3. Funding

Has the project been or will it be peer reviewed?	Yes ☒ No ☐
If yes, by what organisation?	By educational supervisors, named above.
Has funding been sought?	Yes ☐ No ☒
If yes, what is the funding source?	

4. What data is being requested?

Dento- facial	
Oral health	
Audiology	
Perceptual speech	
Psychosocial	
Satisfaction	
Centralisation	
Cropped anonymised images	
Models	X- maxillary only

6. Justification

Please state below the rationale for using CCUK data for this study (including aims and hypotheses) - **limit to half an A4 page.**

Please see attached document.

7. Scientific outline

Please provide a 1 – 2 page outline of your proposal, highlighting the specific requirements of the project for the CCUK data specified above. This needs to include a 250 word summary with keywords.

Please see attached document.

8. Agreement

Please sign below to confirm your agreement to the terms and conditions set out in this document and to certify that the details you have provided are correct.

Signature:	
Date:	18.9.18
Name (on behalf of applicants)	Charlotte Molyneaux

If you are sending this form by email then you should note that in the absence of this signature, the emailing of this proposal constitutes your personal certification that the details are correct.

Please send completed forms to CCUK Study Team (cleftcareuk@uhbristol.nhs.uk).

CCUK Study Team
February 2016
Version 1.1

Cardiff 22 - 24 April 2020

ABSTRACT SUBMISSION TEMPLATE

Cleft, the transverse dimension: CSAG Vs CCUK

Charlotte Molyneaux[1] Martyn Sherriff[2] Anthony Ireland[3]
Jonathan Sandy[4] . University of Bristol

Aim: To determine if the transverse dimensions of maxillary unilateral cleft lip and palate affected children has improved since the implementation of the CSAG recommendations.
Objectives: To deduce the quantitative differences in the arch widths, depths and arch angles between the CSAG and CCUK populations.
Design and Setting: A retrospective cohort study using existing records collected by the CSAG and CCUK studies.
Materials and Methods: The available maxillary models from both the CSAG (114) and CCUK (175) cohorts were digitally scanned and analysed in OrthoAnalyzer™. Measurements recorded were; intercanine and intermolar widths, midline to affected and non-affected side canines and molars, arch length, anterior and posterior palatal depths and archform angle were all recorded.
Results: Agreement analysis was good for all measurements. Of the 11 measurements five showed statistically significant differences between the cohorts where the CSAG measurement was smaller than the CCUK. Those which were clinically significant (>1mm) were the affected side C, affected side E and posterior width.
Conclusions: The null hypotheses are rejected as there was a significant difference between the CSAG and CCUK cohorts for five of the 11 measurements, suggesting that there has been improvement in the maxillary transverse dimension. Changes to surgical protocol, experience and technique may be the reason for this. Where non–cleft norms were available, both the CSAG and CCUK cohorts were reduced for the anterior width, whereas the CCUK cohort was approaching normalisation for the posterior width.